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LOGINID:SSPTAJMN1626

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 7	AUG 27	USPATOLD now available on STN
NEWS 8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 10	SEP 13	FORIS renamed to SOFIS
NEWS 11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 16	OCT 19	BEILSTEIN updated with new compounds
NEWS 17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 18	NOV 19	WPIX enhanced with XML display format
NEWS 19	NOV 30	ICSD reloaded with enhancements
NEWS 20	DEC 04	LINPADOCDB now available on STN
NEWS 21	DEC 14	BEILSTEIN pricing structure to change
NEWS 22	DEC 17	USPATOLD added to additional database clusters
NEWS 23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 24	DEC 17	DGENE now includes more than 10 million sequences
NEWS 25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items

NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:39:09 ON 20 DEC 2007

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 11:39:21 ON 20 DEC 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Dec 2007 VOL 147 ISS 26
FILE LAST UPDATED: 19 Dec 2007 (20071219/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s US 2005-554704/an
L1 0 US 2005-554704/AN

=> s US 2005-554704/ap
L2 1 US 2005-554704/AP
(US2005-554704/AP)

=> sel rn
E1 THROUGH E21 ASSIGNED

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	5.04	5.25

FILE 'REGISTRY' ENTERED AT 11:40:34 ON 20 DEC 2007

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 DEC 2007 HIGHEST RN 958936-22-6
DICTIONARY FILE UPDATES: 19 DEC 2007 HIGHEST RN 958936-22-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s e1-e21
1 113798-74-6/BI
(113798-74-6/RN)
1 131573-78-9/BI
(131573-78-9/RN)
1 145414-58-0/BI
(145414-58-0/RN)
1 153993-80-7/BI
(153993-80-7/RN)
1 261762-50-9/BI
(261762-50-9/RN)
1 343612-72-6/BI
(343612-72-6/RN)
1 625437-42-5/BI
(625437-42-5/RN)
1 790248-42-9/BI
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1 790248-44-1/BI
(790248-44-1/RN)
1 790248-45-2/BI
(790248-45-2/RN)
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1 790248-53-2/BI

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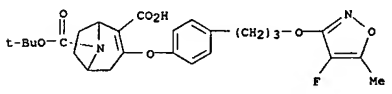
1 9015-94-5/BI
(9015-94-5/RN)
L3 21 (113798-74-6/BI OR 131573-78-9/BI OR 145414-58-0/BI OR 153993-80-7/BI OR 261762-50-9/BI OR 343612-72-6/BI OR 625437-42-5/BI OR 790248-42-9/BI OR 790248-44-1/BI OR 790248-45-2/BI OR 790248-46-3/BI OR 790248-47-4/BI OR 790248-48-5/BI OR 790248-49-6/BI OR 790248-50-9/BI OR 790248-51-0/BI OR 790248-52-1/BI OR 790248-53-2/BI OR 9001-92-7/BI OR 9015-82-1/BI OR 9015-94-5/BI)

=> d l3

L3 ANSWER 1 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-53-2 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-[(4-fluoro-5-methyl-3-isoxazolyl)oxy]propyl]phenoxy]-, 8-(1,1-dimethylethyl) ester (CA INDEX NAME)
MF C26 H31 F N2 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

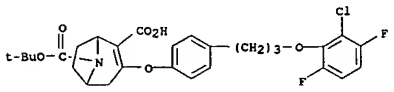


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d l3 2-21

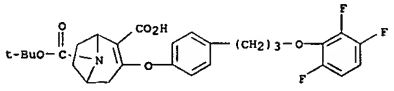
L3 ANSWER 2 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-52-1 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenoxy]-, 8-(1,1-dimethylethyl) ester (CA INDEX NAME)
MF C28 H30 Cl F2 N O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

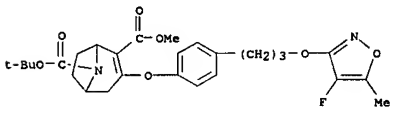
L3 ANSWER 3 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-51-0 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenoxy]-, 8-(1,1-dimethylethyl) ester (CA INDEX NAME)
MF C28 H30 F3 N O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

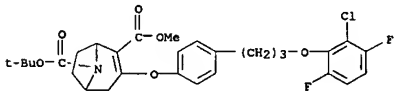
L3 ANSWER 4 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-50-9 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-[(4-fluoro-5-methyl-3-isoxazolyl)oxy]propyl]phenoxy]-, 8-(1,1-dimethylethyl) 2-methyl ester (CA INDEX NAME)
MF C27 H33 F N2 O7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

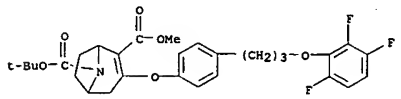
L3 ANSWER 5 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-49-6 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenoxy]-, 8-(1,1-dimethylethyl) 2-methyl ester (CA INDEX NAME)
MF C29 H32 Cl F2 N O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

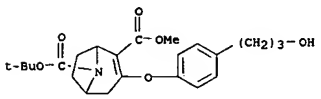
L3 ANSWER 6 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-48-5 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenoxy]-, 8-(1,1-dimethylethyl) 2-methyl ester (CA INDEX NAME)
MF C29 H32 F3 N O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

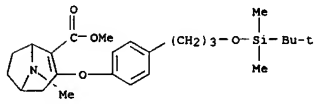
L3 ANSWER 7 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-47-4 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-(3-hydroxypropyl)phenoxy]-, 8-(1,1-dimethylethyl) 2-methyl ester (CA INDEX NAME)
MF C23 H31 N O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 8 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-46-3 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-[4-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]propyl]phenoxy]-8-methyl-, methyl ester (CA INDEX NAME)
MF C25 H39 N O4 Si
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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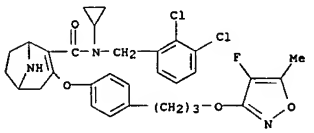
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 9 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-45-2 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-3-[4-[3-[(4-fluoro-5-methyl-3-isoxazolyl)oxy]propyl]phenoxy]- (CA INDEX NAME)
MF C31 H32 Cl2 F N3 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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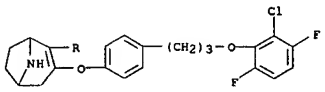
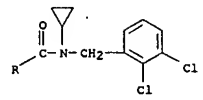
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 10 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-44-1 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenoxy]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)
MF C33 H31 Cl3 F2 N2 O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

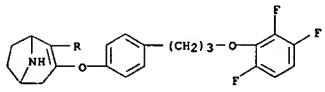


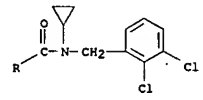


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 11 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 790248-42-9 REGISTRY
ED Entered STN: 29 Nov 2004
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-3-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenoxy]- (CA INDEX NAME)
MF C33 H31 Cl2 F3 N2 O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

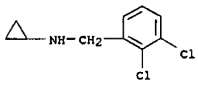




PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

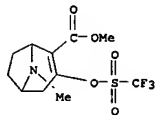
L3 ANSWER 12 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 625437-42-5 REGISTRY
ED Entered STN: 11 Dec 2003
CN Benzenemethanamine, 2,3-dichloro-N-cyclopropyl- (CA INDEX NAME)
OTHER NAMES:
CN (2,3-Dichlorobenzyl)(cyclopropyl)amine
CN Cyclopropyl(2,3-dichlorobenzyl)amine
CN N-Cyclopropyl(2,3-dichlorobenzyl)amine
CN N-Cyclopropyl-2,3-dichlorobenzenemethanamine
CN N-Cyclopropyl-N-(2,3-dichlorobenzyl)amine
MF C10 H11 Cl2 N
SR CA
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

23 REFERENCES IN FILE CA (1907 TO DATE)
23 REFERENCES IN FILE CAPLUS (1907 TO DATE)

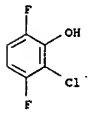
L3 ANSWER 13 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 343612-72-6 REGISTRY
ED Entered STN: 27 Jun 2001
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-3-[[(trifluoromethyl)sulfonyl]oxy]-, methyl ester (CA INDEX NAME)
MF C11 H14 F3 N O5 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

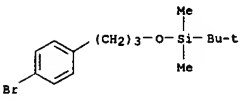
L3 ANSWER 14 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 261762-50-9 REGISTRY
ED Entered STN: 13 Apr 2000
CN Phenol, 2-chloro-3,6-difluoro- (CA INDEX NAME)
OTHER NAMES:
CN 2-Chloro-3,6-difluorophenol
MF C6 H3 Cl F2 O
SR CAS Client Services
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

26 REFERENCES IN FILE CA (1907 TO DATE)
26 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 15 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 153993-80-7 REGISTRY
ED Entered STN: 30 Mar 1994
CN Benzene, 1-bromo-4-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]propyl]-(CA
INDEX NAME)
OTHER CA INDEX NAMES:
CN Silane, [3-(4-bromophenyl)propoxy](1,1-dimethylethyl)dimethyl- (9CI)
OTHER NAMES:
CN [3-(4-Bromophenyl)propoxy](tert-butyl)dimethylsilane
DR 791114-54-0
MF C15 H25 Br O Si
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

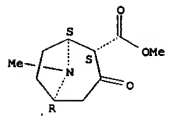


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

21 REFERENCES IN FILE CA (1907 TO DATE)
21 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 16 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 145414-58-0 REGISTRY
ED Entered STN: 21 Jan 1993
CN 8-Azabicyclo[3.2.1]octane-2-carboxylic acid, 8-methyl-3-oxo-, methyl
ester, (1R,2R,5S)-rel- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 8-Azabicyclo[3.2.1]octane-2-carboxylic acid, 8-methyl-3-oxo-, methyl
ester, exo-(±)-
OTHER NAMES:
CN 8-Azabicyclo[3.2.1]octane-2-carboxylic acid, 8-methyl-3-oxo-, methyl
ester, exo-
FS STEREOSEARCH
MF C10 H15 N O3
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

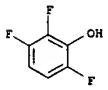
7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 17 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 131573-78-9 REGISTRY
ED Entered STN: 25 Jan 1991
CN 3(2H)-Isoxazolone, 4-fluoro-5-methyl- (CA INDEX NAME)
MF C4 H4 F N O2
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 18 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 113798-74-6 REGISTRY
ED Entered STN: 09 Apr 1988
CN Phenol, 2,3,6-trifluoro- (CA INDEX NAME)
OTHER NAMES:
CN 2,3,6-Trifluorophenol
MF C6 H3 F3 O
CI COM
SR CA
LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

46 REFERENCES IN FILE CA (1907 TO DATE)
46 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 19 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 9015-94-5 REGISTRY
ED Entered STN: 16 Nov 1984
CN Renin (CA INDEX NAME)
OTHER NAMES:
CN Angiotensinogenase
CN E.C. 3.4.23.15
CN E.C. 3.4.4.15
CN E.C. 3.4.99.19
DR 61506-93-2
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MRCK*, NAPRALERT, PROMT, TOXCENTER, USPAT2, USPATFULL, USPATOLD
(*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

18516 REFERENCES IN FILE CA (1907 TO DATE)
48 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
18547 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 20 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 9015-82-1 REGISTRY
ED Entered STN: 16 Nov 1984
CN Carboxypeptidase, dipeptidyl, A (CA INDEX NAME)
OTHER NAMES:
CN ACE
CN ACE (enzyme)
CN Angiotensin I-converting enzyme
CN Angiotensin-1 converting enzyme
CN Angiotensin-converting enzyme
CN Angiotensin-converting enzyme I
CN Angiotension-converting enzyme
CN Carboxycathepsin
CN Carboxypeptidase Zace2
CN Dipeptidyl carboxypeptidase
CN Dipeptidyl carboxypeptidase A
CN Dipeptidyl carboxypeptidase I
CN Dipeptidyl serine carboxypeptidase
CN E.C. 3.4.15.1
CN EC 3.4.15.1
CN Endothelial cell peptidyl dipeptidase
CN Kininase II
CN Peptidase P
CN Peptidyl dipeptidase
CN Peptidyl dipeptidase A
CN Peptidyl dipeptidase-4
CN Peptidyldipeptide hydrolase A
CN Vasopeptidase
CN Zinc metallopeptidase Zacel
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, CSNB, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, PROMT, TOXCENTER, USPAT2, USPATFULL, USPATOLD

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

18498 REFERENCES IN FILE CA (1907 TO DATE)
72 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
18540 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 21 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN
RN 9001-92-7 REGISTRY
ED Entered STN: 16 Nov 1984
CN Proteinase (CA INDEX NAME)
OTHER NAMES:
CN α-N-Benzoyl-DL-arginine-p-nitroanilide hydrolase
CN 537 Acidic protease
CN Actinase
CN AKase IK
CN Alkaline protease-L FG
CN ALP 901
CN Alphamalt BK 5020
CN Alphamalt LQ 4020
CN AO protease
CN APL 901
CN Aquatinase E
CN Arginine esterase
CN Aroase XA 10
CN AS 10
CN Azocaseinase
CN BAPAase
CN BAPNAase
CN Benzoyl arginine arylamidase
CN Benzoyl-DL-arginine-p-nitroanilide hydrolase
CN Bioprase 30L
CN Bioprase SP 4FG
CN Bioprase SP-16FG
CN Bioprotease A
CN Bioprotease N 100P
CN Biopurase
CN Biosoft PW
CN Buzyme 148
CN Buzyme 7705
CN Carbonyl hydrolase
CN Casein endopeptidase
CN Caseinase
CN CL-5PG
CN Cleanase AP 100-PWC
CN Corolase 7089
CN Corolase L 10
CN DA 10
CN DA 10 (enzyme)
CN Denapsin 10P
CN Denatyme AP
CN Denazyme
CN Deozyme
CN Deterzyme L-600
CN Distizym Protacid Extra
CN DQ
CN DQ (enzyme)
CN Durazyme 16.0L
CN E-zyme
CN Endopeptidase
CN Endopeptidase O
CN Endoprotease
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 9001-93-8, 9012-23-1, 9040-76-0, 125498-72-8, 125752-86-5, 123779-18-0, 124041-97-0, 120038-39-3, 120038-40-6, 105913-13-1, 118901-82-9, 144906-30-9, 143404-30-2, 143404-41-5, 80804-52-0, 116267-38-0,

L3 ANSWER 21 OF 21 REGISTRY COPYRIGHT 2007 ACS on STN (Continued)
117278-03-2, 117698-27-8, 118390-80-0, 609346-52-3
MF Unspecified
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, NAPRALERT, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, USPAT2, USPATFULL, USPATOLD
(*File contains numerically searchable property data)
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

46546 REFERENCES IN FILE CA (1907 TO DATE)
552 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
46687 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	43.20	48.45

STN INTERNATIONAL LOGOFF AT 11:43:19 ON 20 DEC 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTANXR1625

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 7	AUG 27	USPATOLD now available on STN
NEWS 8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 10	SEP 13	FORIS renamed to SOFIS
NEWS 11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 16	OCT 19	BEILSTEIN updated with new compounds
NEWS 17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 18	NOV 19	WPIX enhanced with XML display format
NEWS 19	NOV 30	ICSD reloaded with enhancements
NEWS 20	DEC 04	LINPADOCDB now available on STN
NEWS 21	DEC 14	BEILSTEIN pricing structure to change
NEWS 22	DEC 17	USPATOLD added to additional database clusters
NEWS 23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 24	DEC 17	DGENE now includes more than 10 million sequences
NEWS 25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that

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FILE 'HOME' ENTERED AT 08:55:30 ON 26 DEC 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 08:55:39 ON 26 DEC 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 DEC 2007 HIGHEST RN 959463-53-7
DICTIONARY FILE UPDATES: 25 DEC 2007 HIGHEST RN 959463-53-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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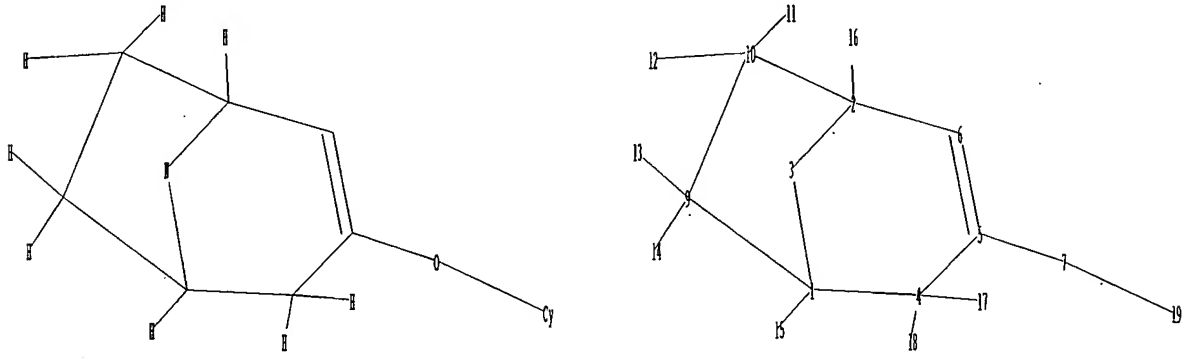
Uploading C:\Program Files\Stnexp\Queries\10544704.str



chain nodes :
7 11 12 13 14 15 16 17 18 19
ring nodes :
1 2 3 4 5 6 9 10
chain bonds :

1-15 2-16 4-17 4-18 5-7 7-19 9-13 9-14 10-11 10-12
ring bonds :
1-4 1-3 1-9 2-6 2-3 2-10 4-5 5-6 9-10
exact/norm bonds :
1-4 1-3 2-6 2-3 4-5 5-6 5-7 7-19
exact bonds :
1-9 1-15 2-10 2-16 4-17 4-18 9-10 9-13 9-14 10-11 10-12
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 9:Atom 10:Atom 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:Atom

L1 STRUCTURE UPLOADED

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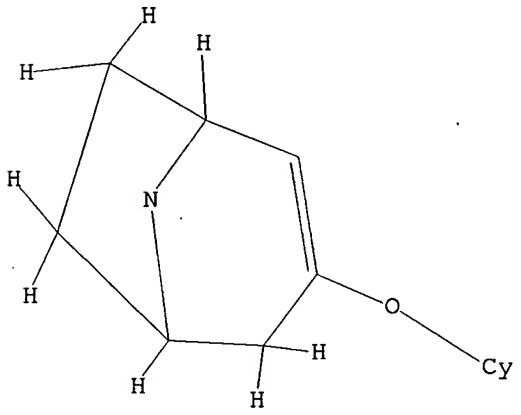
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 937 TO ITERATE

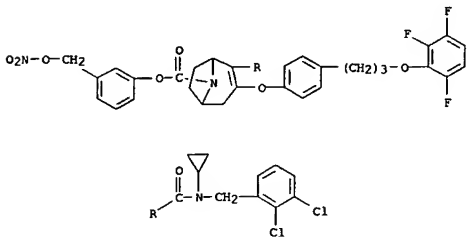
100.0% PROCESSED 937 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 16904 TO 20576
PROJECTED ANSWERS: 3 TO 163

L2 3 SEA SSS SAM L1

=> d scan

L2 3 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN 8-Azabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 2-[[cyclopropyl[(2,3-dichlorophenyl)methyl]amino]carbonyl]-3-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenoxy]-, 3-[(nitrooxy)methyl]phenyl ester
MF C41 H36 Cl2 F3 N3 O8



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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FULL SEARCH INITIATED 08:56:18 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    18056 TO ITERATE

100.0% PROCESSED    18056 ITERATIONS                                20 ANSWERS
SEARCH TIME: 00.00.01

L3           20 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     172.10     172.31

FILE 'CAPLUS' ENTERED AT 08:56:22 ON 26 DEC 2007
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FILE COVERS 1907 - 26 Dec 2007  VOL 147 ISS 26
FILE LAST UPDATED: 25 Dec 2007  (20071225/ED)

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http://www.cas.org/infopolicy.html

=> s l3 full
L4           2 L3

=> d ibib abs hitstr tot
```

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:1064176 CAPLUS
DOCUMENT NUMBER: 147:378417
TITLE: Nonpeptidic organic nitrate compound renin inhibitors, and therapeutic use
INVENTOR(S): Almirante, Nicoletta; Biondi, Stefano; Ongini, Ennio
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 224pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007104652	A2	20070920	WO 2007-EP51933	20070301

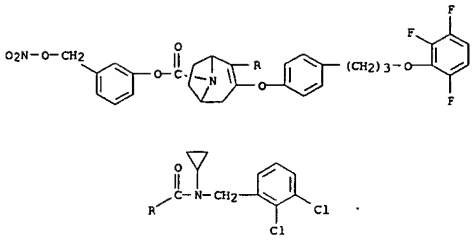
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-782551P P 20060316
OTHER SOURCE(S): MARPAT 147:378417

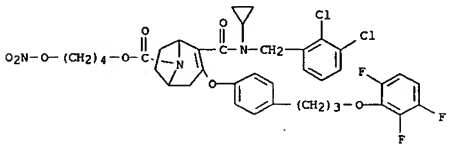
AB The invention discloses nonpeptidic organic nitrate compound renin inhibitors (Markush included) having wider pharmacol. activity and enhanced tolerability. The compds. of the invention can be used for treating or preventing cardiovascular, renal and chronic liver diseases, inflammatory processes and metabolic syndrome.

IT 950484-89-6 950484-90-9 950484-91-0
950484-92-1 950484-93-2 950484-94-3
950484-95-4 950484-96-5 950484-97-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nonpeptidic organic nitrate compound renin inhibitors, therapeutic use, and use with other agents)

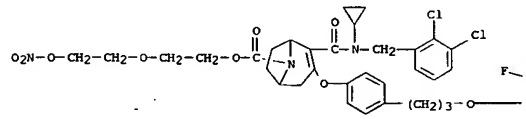
RN 950484-89-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 2-[[cyclopropyl[(2,3-dichlorophenyl)methyl]amino]carbonyl]-3-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenoxy]-, 3-[(nitrooxy)methyl]phenyl ester (CA INDEX NAME)



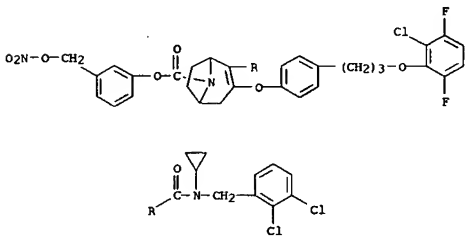
RN 950484-90-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 2-[[cyclopropyl[(2,3-dichlorophenyl)methyl]amino]carbonyl]-3-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenoxy]-, 4-(nitrooxy)butyl ester (CA INDEX NAME)



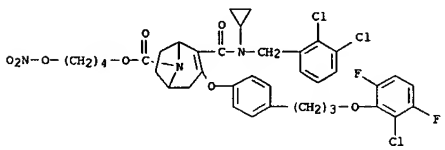
RN 950484-91-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 2-[[cyclopropyl[(2,3-dichlorophenyl)methyl]amino]carbonyl]-3-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenoxy]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (CA INDEX NAME)



RN 950484-92-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenoxy]-2-[[cyclopropyl[(2,3-dichlorophenyl)methyl]amino]carbonyl]-, 3-[(nitrooxy)methyl]phenyl ester (CA INDEX NAME)



RN 950484-93-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenoxy]-2-[[cyclopropyl[(2,3-dichlorophenyl)methyl]amino]carbonyl]-, 4-(nitrooxy)butyl ester (CA INDEX NAME)



RN 950484-94-3 CAPLUS
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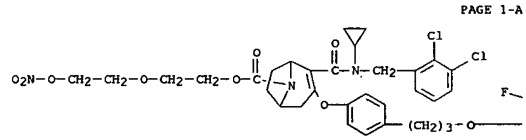
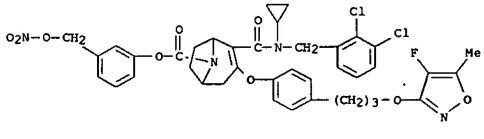
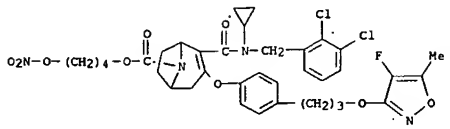


RN 950484-95-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 2-[[cyclopropyl[(2,3-dichlorophenyl)methyl]amino]carbonyl]-3-[4-[3-[(4-fluoro-5-methyl-3-isoxazolyl)oxy]propyl]phenoxy]-, 3-[(nitrooxy)methyl]phenyl ester (CA INDEX NAME)



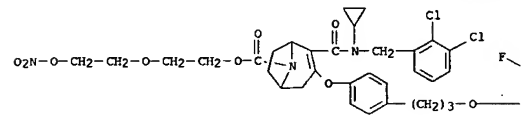
RN 950484-96-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 2-[[cyclopropyl[(2,3-dichlorophenyl)methyl]amino]carbonyl]-3-[4-[3-[(4-fluoro-5-methyl-3-isoxazolyl)oxy]propyl]phenoxy]-, 4-(nitrooxy)butyl ester (CA INDEX NAME)

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 950484-97-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-8-carboxylic acid, 2-[[cyclopropyl[(2,3-dichlorophenyl)methyl]amino]carbonyl]-3-[4-[3-[(4-fluoro-5-methyl-3-isoxazolyl)oxy]propyl]phenoxy]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:965246 CAPLUS
DOCUMENT NUMBER: 141:395703
TITLE: Tropane derivatives and their use as ace inhibitors
INVENTOR(S): Bezencon, Olivier; Bur, Daniel; Fischli, Walter; Remen, Lubos; Richard-Bildstein, Sylvia; Weller, Thomas; Sifferlen, Thierry
PATENT ASSIGNEE(S): Actelion Pharmaceuticals Ltd., Switz.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096799	A1	20041111	WO 2004-EP4375	20040426
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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CA 2521957	A1	20041111	CA 2004-2521957	20040426
EP 1622901	A1	20060208	EP 2004-729423	20040426
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CN 1780833	A	20060531	CN 2004-80011442	20040426
JP 2006524657	T	20061102	JP 2006-505264	20040426
MX 2005PA11497	A	20051215	MX 2005-PA11497	20051025
US 2006205768	A1	20060914	US 2005-554704	20051027
NO 2005005624	A	20051129	NO 2005-5624	20051129
IN 2005CN03209	A	20070831	IN 2005-CN3209	20051130
PRIORITY APPLN. INFO.:			WO 2003-EP304490 A	20030430
			WO 2004-EP4375 W	20040426
OTHER SOURCE(S):	MARPAT 141:395703			

GI

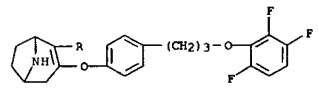
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

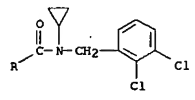
AB The invention relates to the preparation of tropane derivs., I (W = a six-membered, non benzofused, Ph or heteroaryl ring substituted by V in the meta or para position; V = alkyl, alkoxy, sulfoxy, sulfide, ether, etc.; U = aryl, heteroaryl; T = amide, ester sulfamide; Q = lower alkylene, lower alkenylene; M = H, cycloalkyl, aryl, heterocycle, heteroaryl), and their use as active ingredients in the preparation of pharmaceutical compns. as ACE and renin inhibitors for the potential treatment of related cardiovascular and renal diseases. Thus, II was treated with NaH and Tf2NPh to give the corresponding triflate. The triflate was then coupled with [3-(4-bromophenyl)propoxy]-tert-

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
butyldimethylsilane and ZnCl2, followed by demethylation, Boc-protection, and coupling with 2,3,6-trifluoropehnol gives III (R = COOCMe3), which was further reacted with cyclopropyl-(2,3-dichloro-benzyl)amine to give IV.

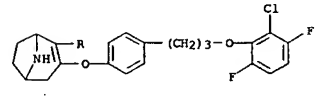
IT 790248-42-9P 790248-44-1P 790248-45-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tropane derivs. and their use as renin and ace inhibitors for the treatment of cardiovascular disease, renal diseases, and other related conditions)

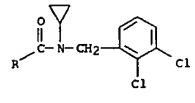
RN 790248-42-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-3-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenoxy]- (CA INDEX NAME)





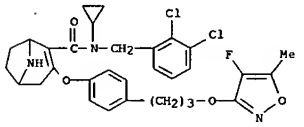
RN 790248-44-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenoxy]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)





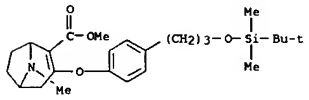
RN 790248-45-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-3-[4-[3-[(4-fluoro-5-methyl-3-isoxazolyl)oxy]propyl]phenoxy]- (CA INDEX NAME)

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

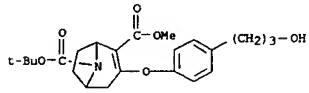


IT 790248-46-3P 790248-47-4P 790248-48-5P
790248-49-6P 790248-50-9P 790248-51-0P
790248-52-1P 790248-53-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of tropane derivs. and their use as renin and ace inhibitors for the treatment of cardiovascular disease, renal diseases, and other related conditions)

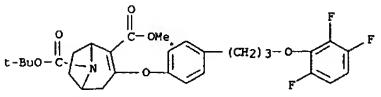
RN 790248-46-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-[4-[3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]propyl]phenoxy]-8-methyl-, methyl ester (CA INDEX NAME)



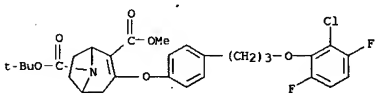
RN 790248-47-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-(3-hydroxypropyl)phenoxy]-, 8-(1,1-dimethylethyl) 2-methyl ester (CA INDEX NAME)



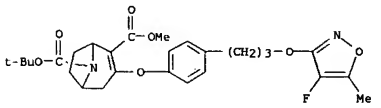
RN 790248-48-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenoxy]-, 8-(1,1-dimethylethyl) 2-methyl ester (CA INDEX NAME)



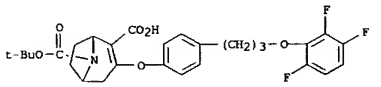
RN 790248-49-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenoxy]-, 8-(1,1-dimethylethyl) 2-methyl ester (CA INDEX NAME)



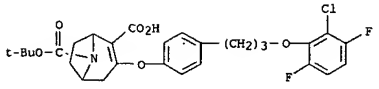
RN 790248-50-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-[(4-fluoro-5-methyl-3-isoxazolyl)oxy]propyl]phenoxy]-, 8-(1,1-dimethylethyl) 2-methyl ester (CA INDEX NAME)



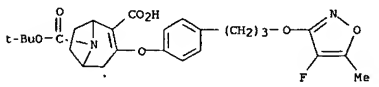
RN 790248-51-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-(2,3,6-trifluorophenoxy)propyl]phenoxy]-, 8-(1,1-dimethylethyl) ester (CA INDEX NAME)



RN 790248-52-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenoxy]-, 8-(1,1-dimethylethyl) ester (CA INDEX NAME)



RN 790248-53-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2,8-dicarboxylic acid, 3-[4-[3-[(4-fluoro-5-methyl-3-isoxazolyl)oxy]propyl]phenoxy]-, 8-(1,1-dimethylethyl) ester (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L1              STRUCTURE UPLOADED
L2            3 S L1
L3           20 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 08:56:22 ON 26 DEC 2007
L4            2 S L3 FULL

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FULL ESTIMATED COST                                    11.01     183.32

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                    -1.56      -1.56

STN INTERNATIONAL LOGOFF AT 08:57:04 ON 26 DEC 2007
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Connecting via Winsock to STN

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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 7	AUG 27	USPATOLD now available on STN
NEWS 8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 10	SEP 13	FORIS renamed to SOFIS
NEWS 11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 16	OCT 19	BEILSTEIN updated with new compounds
NEWS 17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 18	NOV 19	WPIX enhanced with XML display format
NEWS 19	NOV 30	ICSD reloaded with enhancements
NEWS 20	DEC 04	LINPADOCDB now available on STN
NEWS 21	DEC 14	BEILSTEIN pricing structure to change
NEWS 22	DEC 17	USPATOLD added to additional database clusters
NEWS 23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 24	DEC 17	DGENE now includes more than 10 million sequences
NEWS 25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 07:26:41 ON 20 DEC 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 07:26:50 ON 20 DEC 2007
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 DEC 2007 HIGHEST RN 958936-22-6
DICTIONARY FILE UPDATES: 19 DEC 2007 HIGHEST RN 958936-22-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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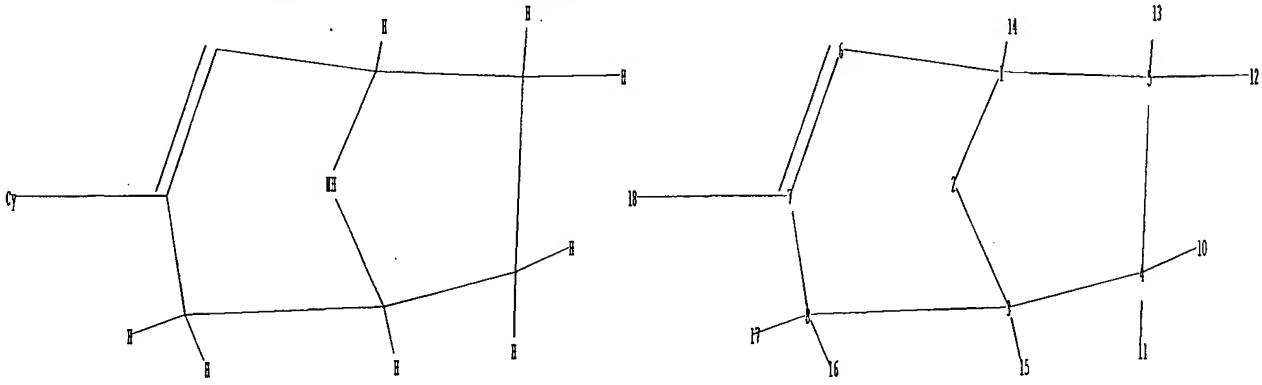
Uploading C:\Program Files\Stnexp\Queries\10554704.str



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10 11 12 13 14 15 16 17 18
ring nodes :
1 2 3 4 5 6 7 8

chain bonds :
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ring bonds :
1-2 1-5 1-6 2-3 3-4 3-8 4-5 6-7 7-8
exact/norm bonds :
1-2 1-6 2-3 3-8 6-7 7-18 7-8
exact bonds :
1-5 1-14 3-4 3-15 4-5 4-10 4-11 5-12 5-13 8-16 8-17
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 10:CLASS 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:Atom
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18:
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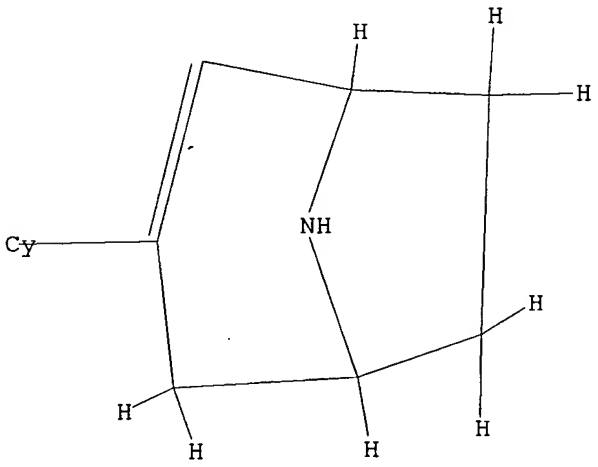

Structure attributes must be viewed using STN Express query preparation.

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FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 43569 TO 49351
PROJECTED ANSWERS: 4 TO 221

L2 4 SEA SSS SAM L1

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SEARCH TIME: 00.00.01

L3 155 SEA SSS FUL L1

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COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 172.10 172.31

FILE 'CAPLUS' ENTERED AT 07:27:16 ON 20 DEC 2007
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FILE COVERS 1907 - 20 Dec 2007 VOL 147 ISS 26
FILE LAST UPDATED: 19 Dec 2007 (20071219/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

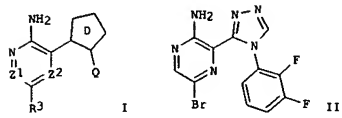
=> s l3 full
L4 37 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:1116839 CAPLUS
DOCUMENT NUMBER: 147:427360
TITLE: Preparation of tetrazolyl (or triazolyl) substituted pyridinamines or pyrimidinamines as c-Met protein kinase inhibitors
INVENTOR(S): Lauffer, David J.; Davies, Robert J.; Stamos, Dean; Aronov, Alexander; Deininger, David D.; Grey, Ronald, Jr.; Xu, Jinwang; Li, Pan; Ledford, Brian; Farmer, Luc; Bethiel, Randy Scott; Jacobs, Dylan; Mcginty, Kira
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 254pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007111904	A2	20071004	WO 2007-US7016	20070321
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007254868	A1	20071101	US 2007-726170	20070321
PRIORITY APPLN. INFO.:			US 2006-784937P P	20060322
			US 2006-875973P P	20061220

OTHER SOURCE(S): MARPAT 147:427360
GI



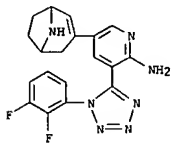
I II

AB The title compds. I [Z1 = N or CR4; Z2 = N or CH; ring D = triazolyl, tetrazolyl, etc.; Q = (un)substituted 6-10 membered aryl or 5-10 membered heteroaryl; R3 = halo, (un)substituted aryl, heteroaryl, etc.; R4 = H, alkyl, halo or haloalkyl], useful as c-Met protein kinase inhibitors, were prepared E.g., a multi-step synthesis of II, starting from 3-aminopyrazine-2-carboxylic acid and 2,3-difluoroaniline, was given. Exemplified compds. I were tested for inhibition of c-MET (data given).

L4 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
The invention also provides processes for prepg. the compds. I, pharmaceutically acceptable compns. comprising the compds. I, and methods of using the compns. in the treatment of various disorders.

IT 951258-24-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tetrazolyl (or triazolyl) substituted pyridinamines or pyrimidinamines as c-Met protein kinase inhibitors for treating proliferative disorders)

RN 951258-24-5 CAPLUS
CN 2-Pyridinamine, 5-(8-azabicyclo[3.2.1]oct-2-en-3-yl)-3-[1-(2,3-difluorophenyl)-1H-tetrazol-5-yl]- (CA INDEX NAME)



L4 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:874593 CAPLUS
DOCUMENT NUMBER: 147:257666
TITLE: Preparation of secondary amines as renin inhibitors
INVENTOR(S): Bezencon, Olivier; Bur, Daniel; Corminboeuf, Olivier; Dube, Daniel; Grisostomi, Corinna; MacDonald, Dwight; McKay, Dan; Powell, David; Remen, Lubos; Richard-Bildstein, Sylvia; Scheigetz, John; Therien, Michel; Weller, Thomas
PATENT ASSIGNEE(S): Actelion Pharmaceuticals Ltd., Switz.
SOURCE: PCT Int. Appl., 236pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007088514	A1	20070809	WO 2007-IB50327	20070131
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			WO 2006-IB50356 A	20060202

OTHER SOURCE(S): MARPAT 147:257666
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

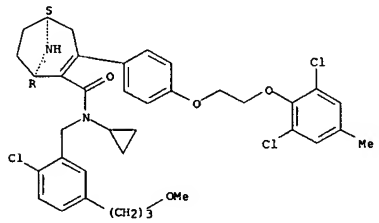
AB Title compds. represented by the formula I [wherein X = CH, N or N+-O-; W = para-substituted Ph or pyridinyl, or thiazolyl; V = -CH2CH2CH2-, -CH2CH2-O-, -CH2-S-CH2-, etc.; U = (un)substituted aryl; R1 = (cyclo)alkyl, R2 = halo or alkyl; R3 = H, alkyl, alkoxy, CF3 or halo; R4 = alkyl-O-CH2-, CF3-O-CH2-CH2-, -NH-CH2-, etc.; L = -CH2-CH2-, -CH2-CH2-CH2-, -CH2-O-CH2-, etc.; n = 0 or 1; and pharmaceutically acceptable salts thereof] were prepared as renin inhibitors. For example, reaction of (1R*,5S*)-7-[4-[2-(2,6-dichloro-4-methylphenoxy)ethyl]phenyl]-3,9-diazabicyclo[3.3.1]non-6-ene-3,6,9-tricarboxylic acid 3,9-di-tert-Bu ester with [2-chloro-5-(3-methoxypropyl)benzyl](cyclopropyl)amine and followed by hydrolysis, gave II. II showed renin inhibition with IC50 value of 0.2 nM in enzyme immuno assay. Thus, I and their pharmaceutical compns. are useful as renin inhibitors for the treatment and/or prophylaxis of diseases, such as hypertension, congestive, heart failure, and etc.

IT 945996-42-9P 945996-54-3P 945996-63-4P
945996-86-1P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L4 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(prepn. of azabicyclo[3.2.1]octane and hexahydrobipyridine carboxamide derivs. as renin inhibitors)

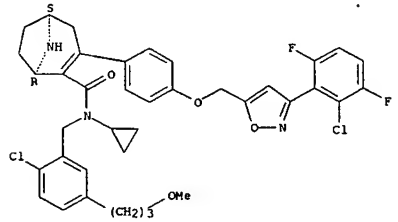
RN 945996-42-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-[[2-chloro-5-(3-methoxypropyl)phenyl]methyl]-N-cyclopropyl-3-[4-[2-(2,6-dichloro-4-methylphenoxy)ethoxy]phenyl]-, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.



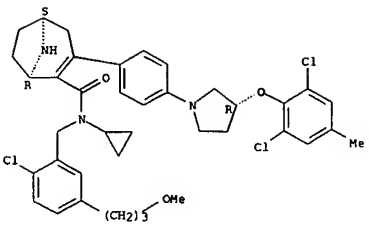
RN 945996-54-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[4-[[3-(2-chloro-3,6-difluorophenyl)-5-isoxazolyl]methoxy]phenyl]-N-[[2-chloro-5-(3-methoxypropyl)phenyl]methyl]-N-cyclopropyl-, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.



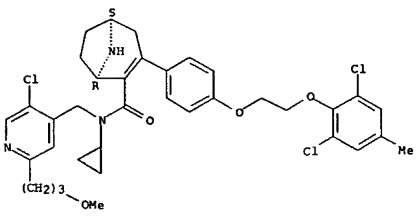
RN 945996-63-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-[[2-chloro-5-(3-methoxypropyl)phenyl]methyl]-N-cyclopropyl-3-[4-[(3R)-3-(2,6-dichloro-4-methylphenoxy)-1-pyrrolidinyl]phenyl]-, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.



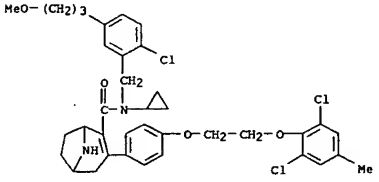
RN 945996-86-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-[[5-chloro-2-(3-methoxypropyl)-4-pyridinyl]methyl]-N-cyclopropyl-3-[4-[2-(2,6-dichloro-4-methylphenoxy)ethoxy]phenyl]-, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.

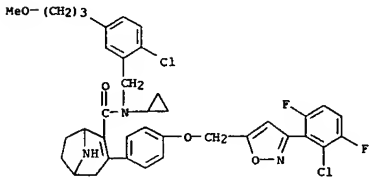


IT 945996-61-2P 945996-62-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azabicyclo[3.2.1]octane and hexahydrobipyridine carboxamide
derivs. as renin inhibitors)
RN 945996-61-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-[[2-chloro-5-(3-methoxypropyl)phenyl]methyl]-N-cyclopropyl-3-[6-[2-(2,6-dichloro-4-methylphenoxy)ethoxy]-3-pyridinyl]-, (1R,5S)- (CA INDEX NAME)

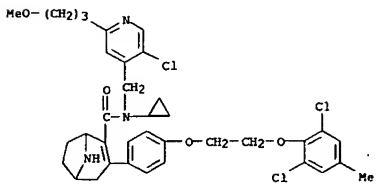
Absolute stereochemistry..



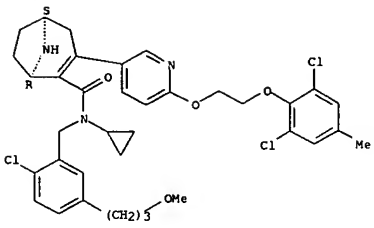
RN 945998-41-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[4-[[3-(2-chloro-3,6-difluorophenyl)-5-isoxazolyl]methoxy]phenyl]-N-[[2-chloro-5-(3-methoxypropyl)phenyl]methyl]-N-cyclopropyl- (CA INDEX NAME)



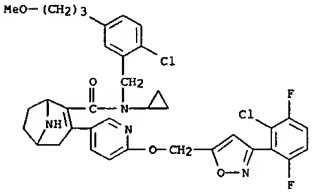
RN 945998-70-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-[[5-chloro-2-(3-methoxypropyl)-4-pyridinyl]methyl]-N-cyclopropyl-3-[4-[2-(2,6-dichloro-4-methylphenoxy)ethoxy]phenyl]- (CA INDEX NAME)



IT 945998-49-2P 946004-31-5P
RL: SPN (Synthetic preparation); PREP (Preparation)



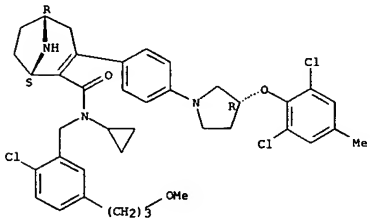
RN 945996-62-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[6-[[3-(2-chloro-3,6-difluorophenyl)-5-isoxazolyl]methoxy]-3-pyridinyl]-N-[[2-chloro-5-(3-methoxypropyl)phenyl]methyl]-N-cyclopropyl- (CA INDEX NAME)



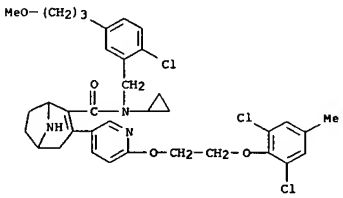
IT 945998-27-6P 945998-41-4P 945998-70-9P
RL: PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(preparation of azabicyclo[3.2.1]octane and hexahydrobipyridine carboxamide
derivs. as renin inhibitors)
RN 945998-27-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-[[2-chloro-5-(3-methoxypropyl)phenyl]methyl]-N-cyclopropyl-3-[4-[2-(2,6-dichloro-4-methylphenoxy)ethoxy]phenyl]- (CA INDEX NAME)

RN 945998-49-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-[[2-chloro-5-(3-methoxypropyl)phenyl]methyl]-N-cyclopropyl-3-[4-[(3R)-3-(2,6-dichloro-4-methylphenoxy)-1-pyrrolidinyl]phenyl]-, (1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 946004-31-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-[[2-chloro-5-(3-methoxypropyl)phenyl]methyl]-N-cyclopropyl-3-[6-[2-(2,6-dichloro-4-methylphenoxy)ethoxy]-3-pyridinyl]- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

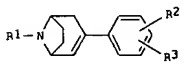
L4 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:259642 CAPLUS
DOCUMENT NUMBER: 146:316780
TITLE: Azabicyclo[3.2.1]oct-2-ene derivatives as monoamine neurotransmitter re-uptake inhibitors, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Peters, Dan; Dahl, Bjarne H.; Redrobe, John Paul; Nielsen, Elsebet Oestergaard
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 27pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007025978	A1	20070308	WO 2006-EP65804	20060830

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: DK 2005-1218 A 20050901
US 2005-713367P P 20050902
OTHER SOURCE(S): MARPAT 146:316780
GI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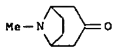
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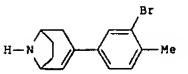
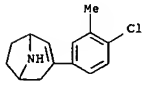

III

L4 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB The invention relates to azabicyclo[3.2.1]oct-2-enes of formula I, which are monoamine neurotransmitter re-uptake inhibitors. In compds. I, R1 is H or (un)substituted alkyl; R2 is alkyl; and R3 is selected from halo, OH, NH2, cyano, nitro, trifluoromethyl, trifluoromethoxy, alkoxy, cycloalkoxy, alkoxyalkyl, cycloalkoxyalkyl, alkyl, cycloalkyl, cycloalkyl-alkyl, alkenyl, alkynyl, (di)alkylamino, (un)substituted carbamoyl, and (un)substituted acylamino; including isomers, mixts. of isomers, and pharmaceutically acceptable salts thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I together with at least one pharmaceutically acceptable carrier, excipient, or diluent, as well as to the use of the compns. for the treatment of CNS disorders, including depression and panic disorder. Bromine-lithium exchange of 2,4-dibromotoluene followed by addition to tropinone (II), dehydration, and N-demethylation gave azabicyclooctene III. The compds. of the invention are monoamine neurotransmitter re-uptake inhibitors, e.g., compound III expresses IC50 values of 13 nM, 15 nM, and 1.4 nM for inhibition of uptake of dopamine, noradrenaline, and serotonin, resp.

IT 928266-37-9P, 3-(4-Chloro-3-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of azabicyclooctene derivs. as monoamine neurotransmitter reuptake inhibitors)

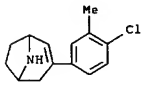
RN 928266-37-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chloro-3-methylphenyl)- (CA INDEX NAME)



IT 928266-36-8P, 3-(4-Chloro-3-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene hydrochloride 928266-40-4P, 3-(3-Chloro-4-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene hydrochloride 928266-41-5P, 3-(3,4-Dimethylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene hydrochloride 928266-42-6P, 3-(2,3-Dimethylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene hydrochloride 928266-43-7P, 3-(3-Fluoro-4-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene hydrochloride 928266-44-8P, 3-(4-Fluoro-3-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene hydrochloride 928266-45-9P, 3-(4-Chloro-3-ethylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene hydrochloride 928266-46-0P, 3-(3-Chloro-4-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene 928266-47-1P 928266-48-2P 928266-49-3P 928266-50-6P 928266-51-7P, 3-(4-Chloro-3-ethylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene 928266-52-8P 928266-53-9P, 3-(4-Bromo-3-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene hydrochloride 928266-54-0P, 3-(3-Bromo-4-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene hydrochloride 928266-75-5P, 3-(3,4-Dimethylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene 928266-76-6P, 3-(2,3-Dimethylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene 928266-77-7P, 3-(3-Fluoro-4-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene 928266-78-8P, 3-(4-Fluoro-3-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene 928266-79-9P 928266-80-2P 928266-81-3P 928266-82-4P 928266-83-5P 928266-84-6P, 3-(4-Bromo-3-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene 928266-85-7P, 3-(3-Bromo-4-methylphenyl)-8H-8-azabicyclo[3.2.1]oct-2-ene
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of azabicyclooctene derivs. as monoamine neurotransmitter reuptake inhibitors)

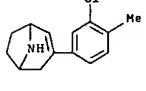
L4 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 928266-36-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chloro-3-methylphenyl)-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

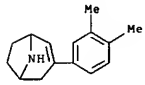
RN 928266-40-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chloro-4-methylphenyl)-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

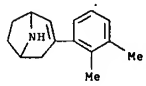
RN 928266-41-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dimethylphenyl)-, hydrochloride (1:1) (CA INDEX NAME)

L4 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



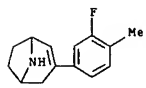
● HCl

RN 928266-42-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2,3-dimethylphenyl)-, hydrochloride (1:1) (CA INDEX NAME)



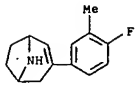
● HCl

RN 928266-43-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-fluoro-4-methylphenyl)-, hydrochloride (1:1) (CA INDEX NAME)



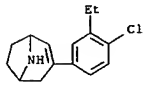
● HCl

RN 928266-44-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-fluoro-3-methylphenyl)-, hydrochloride (1:1) (CA INDEX NAME)



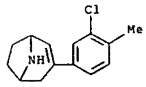
● HCl

RN 928266-45-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chloro-3-ethylphenyl)-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

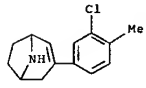
RN 928266-46-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chloro-4-methylphenyl)- (CA INDEX NAME)

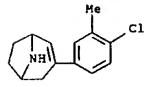


RN 928266-47-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chloro-4-methylphenyl)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 928266-46-0
CMF C14 H16 Cl N

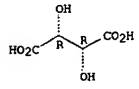




CM 2

CRN 87-69-4
CMF C4 H6 O6

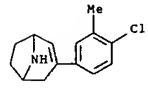
Absolute stereochemistry.



RN 928266-50-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chloro-3-methylphenyl)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (CA INDEX NAME)

CM 1

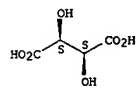
CRN 928266-37-9
CMF C14 H16 Cl N



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.

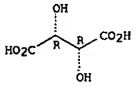


RN 928266-51-7 CAPLUS

CM 2

CRN 87-69-4
CMF C4 H6 O6

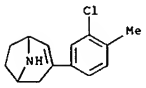
Absolute stereochemistry.



RN 928266-48-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chloro-4-methylphenyl)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (CA INDEX NAME)

CM 1

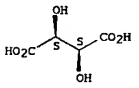
CRN 928266-46-0
CMF C14 H16 Cl N



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.

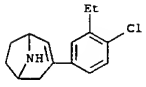


RN 928266-49-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chloro-3-methylphenyl)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (CA INDEX NAME)

CM 1

CRN 928266-37-9
CMF C14 H16 Cl N

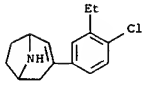
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chloro-3-ethylphenyl)- (CA INDEX NAME)



RN 928266-52-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chloro-3-ethylphenyl)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (CA INDEX NAME)

CM 1

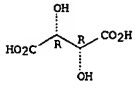
CRN 928266-51-7
CMF C15 H18 Cl N



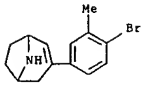
CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

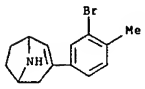


RN 928266-53-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-bromo-3-methylphenyl)-, hydrochloride (1:1) (CA INDEX NAME)



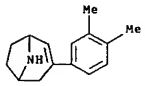
● HCl

RN 928266-54-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-bromo-4-methylphenyl)-, hydrochloride (1:1) (CA INDEX NAME)

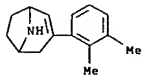


● HCl

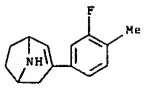
RN 928266-75-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dimethylphenyl)- (CA INDEX NAME)



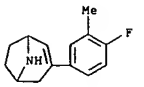
RN 928266-76-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2,3-dimethylphenyl)- (CA INDEX NAME)



RN 928266-77-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-fluoro-4-methylphenyl)- (CA INDEX NAME)

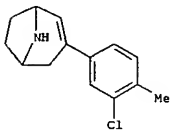


RN 928266-78-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-fluoro-3-methylphenyl)- (CA INDEX NAME)



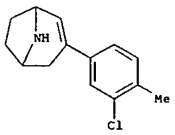
RN 928266-79-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chloro-4-methylphenyl)-, (-)- (CA INDEX NAME)

Rotation (-).



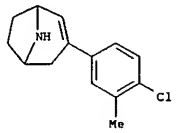
RN 928266-80-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chloro-4-methylphenyl)-, (+)- (CA INDEX NAME)

Rotation (+).



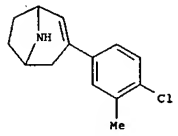
RN 928266-81-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chloro-3-methylphenyl)-, (-)- (CA INDEX NAME)

Rotation (-).



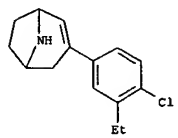
RN 928266-82-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chloro-3-methylphenyl)-, (+)- (CA INDEX NAME)

Rotation (+).

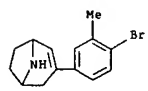


RN 928266-83-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chloro-3-ethylphenyl)-, (-)- (CA INDEX NAME)

Rotation (-).

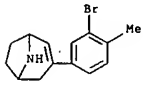


RN 928266-84-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-bromo-3-methylphenyl)- (CA INDEX NAME)



RN 928266-85-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-bromo-4-methylphenyl)- (CA INDEX NAME)



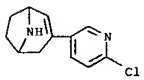
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1188389 CAPLUS
DOCUMENT NUMBER: 146:100761
TITLE: Suzuki couplings of new bicyclic boronic esters derived from 8-heterobicyclo[3.2.1]octenyl nonaflates and application to the synthesis of an epibatidine-atropine hybrid
AUTHOR(S): Hoegermeier, Jens; Reissig, Hans-Ulrich
CORPORATE SOURCE: Institut fuer Chemie und Biochemie, Freie Universitaet Berlin, Berlin, 14165, Germany
SOURCE: Synlett (2006), (17), 2759-2762
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:100761

AB Palladium-catalyzed reactions of alkenyl nonaflates derived from 8-oxabicyclo[3.2.1]octan-3-ones with bis(pinacolato)diboron as coupling partner led to bicyclic boronic esters. They were further transformed in a subsequent coupling step either using iodobenzene or a second equivalent of the corresponding bicyclic alkenyl nonaflate. Products were obtained in reasonable to fair yields. Applying this method to N-carbethoxytropinone derived nonaflate provided an epibatidine-atropine hybrid in only three steps with 65% overall yield.

IT 259522-30-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(Suzuki couplings of new bicyclic boronic esters derived from heterobicyclooctenyl nonaflates and application to preparation of epibatidine-atropine hybrid)

RN 259522-30-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(6-chloro-3-pyridinyl)- (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

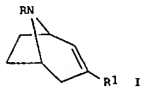
L4 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1091087 CAPLUS
DOCUMENT NUMBER: 145:438794
TITLE: Novel enantiomers and their use as monoamine neurotransmitter re-uptake inhibitors
INVENTOR(S): Peters, Dan; Dahl, Bjarne H.; Olesen, Dorthe Filtenborg; Nielsen, Elsebet Oestergaard; Olsen, Gunnar M.; Redrobe, John Paul
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 30pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006108789	A1	20061019	WO 2006-EP61363	20060406

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: DK 2005-505 A 20050408
US 2005-669918P P 20050411
DK 2005-1572 A 20051111
US 2005-736331P P 20051115

OTHER SOURCE(S): MARPAT 145:438794
GI

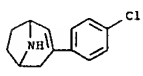


AB 8-Azabicyclo[3.2.1]oct-2-ene derivs., such as I [R = H, alkyl; R1 = acyl], were prepared for therapeutic use in the treatment, prevention or alleviation of diseases, disorders or conditions which are responsive to inhibition of monoamine neurotransmitter re-uptake in the central nervous system. These compds. were claimed for use in the treatment of mood disorder, depression, atypical depression, depression secondary to pain, major depressive disorder, dysthymic disorder, bipolar disorder, bipolar I disorder, bipolar II disorder, cyclothymic disorder, mood disorder due to a general medical condition, substance-induced mood disorder, pseudodementia, Ganser's syndrome, obsessive compulsive disorder, panic disorder, panic disorder without agoraphobia, panic disorder with agoraphobia, agoraphobia without history of panic disorder, panic attack, memory deficits, memory loss, attention deficit hyperactivity disorder,

L4 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
obesity, anxiety, generalized anxiety disorder, eating disorder, Parkinson's disease, parkinsonism, dementia, dementia of aging, senile dementia, Alzheimer's disease, acquired immunodeficiency syndrome dementia complex, memory dysfunction in aging, specific phobia, social phobia, social anxiety disorder, posttraumatic stress disorder, acute stress disorder drug addiction, drug abuse, cocaine abuse, nicotine abuse, tobacco abuse, alc. addiction, alcoholism and kleptomania. These compds. were also claimed for use in the treatment of pain, chronic pain, inflammatory pain, neuropathic pain, migraine pain, tension-type headache, chronic tension-type headache, pain assocd. with depression, fibromyalgia, arthritis, osteoarthritis, rheumatoid arthritis, back pain, cancer pain, irritable bowel pain, irritable bowel syndrome, postoperative pain, post-mastectomy pain syndrome (PMPS), post-stroke pain, drug-induced neuropathy, diabetic neuropathy, sympathetically-maintained pain, trigeminal neuralgia, dental pain, myofacial pain, phantom-limb pain, bulimia, premenstrual syndrome, premenstrual dysphoric disorder, late luteal phase syndrome, posttraumatic syndrome, chronic fatigue syndrome, urinary incontinence, stress incontinence, urge incontinence, nocturnal incontinence, sexual dysfunction, premature ejaculation, erectile difficulty, erectile dysfunction, premature female orgasm, restless leg syndrome, periodic limb movement disorder, eating disorders, anorexia nervosa, sleep disorders, pervasive developmental disorders, autism, Asperger's disorder, Rett's disorder, childhood disintegrative disorder, learning disabilities, motor skills disorders, mutism, trichotillomania, narcolepsy, post-stroke depression, stroke-induced brain damage, stroke-induced neuronal damage, Gilles de la Tourettes disease, tinnitus, tic disorders, body dysmorphic disorders, oppositional defiant disorder or post-stroke disabilities. Thus, the (-)-enantiomer of 3-(4-Chlorophenyl)-8-methyl-8-azabicyclo[3.2.1]oct-2-ene I (R = Me, R2 = C6H4-4-Cl) was prepd. as its hydrochloride salt via an arylation reaction of the (-)-enantiomer of triflate I (R = Me, R1 = OSO2CF3) with Cl-4-C6H4-B(OH)2 using Pd(PPh3)4, potassium carbonate and LiCl in (CH2OMe)2 and H2O. The prepd. compds. were tested for inhibition of re-uptake of the dopamine, noradrenaline and serotonin monoamine neurotransmitters.

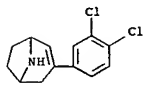
IT 189746-53-0P 189746-56-3P 912641-10-2P
912641-12-4P 912641-14-6P 912641-16-8P
912641-18-0P 912641-21-5P 912641-23-7P
912641-26-0P 912641-29-3P 912642-09-2P
912642-11-6P 912642-14-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; enantioselective preparation of 8-azabicyclo[3.2.1]oct-2-ene derivs. for therapeutic use as monoamine neurotransmitter re-uptake inhibitors)

RN 189746-53-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chlorophenyl)- (CA INDEX NAME)



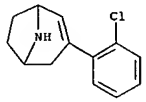
RN 189746-56-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dichlorophenyl)- (CA INDEX NAME)

L4 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



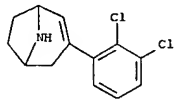
RN 912641-10-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2-chlorophenyl)-, (+)- (CA INDEX NAME)

Rotation (+).



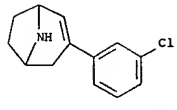
RN 912641-12-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2,3-dichlorophenyl)-, (+)- (CA INDEX NAME)

Rotation (+).



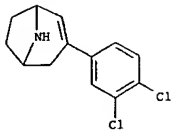
RN 912641-14-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chlorophenyl)-, (+)- (CA INDEX NAME)

Rotation (+).



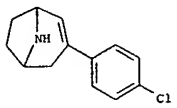
RN 912641-16-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dichlorophenyl)-, (+)- (CA INDEX NAME)

Rotation (+).



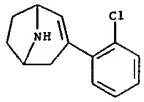
RN 912641-18-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chlorophenyl)-, (-)- (CA INDEX NAME)

Rotation (-).



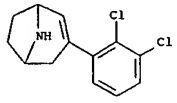
RN 912641-21-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2-chlorophenyl)-, (-)- (CA INDEX NAME)

Rotation (-).



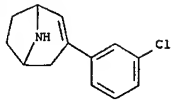
RN 912641-23-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2,3-dichlorophenyl)-, (-)- (CA INDEX NAME)

Rotation (-).



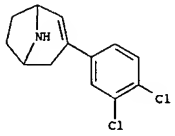
RN 912641-26-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chlorophenyl)-, (-)- (CA INDEX NAME)

Rotation (-).

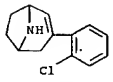


RN 912641-29-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dichlorophenyl)-, (-)- (CA INDEX NAME)

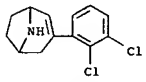
Rotation (-).



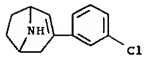
RN 912642-09-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2-chlorophenyl)- (CA INDEX NAME)



RN 912642-11-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2,3-dichlorophenyl)- (CA INDEX NAME)



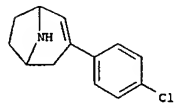
RN 912642-14-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chlorophenyl)- (CA INDEX NAME)



IT 912641-08-8P 912641-09-9P 912641-11-3P
912641-13-5P 912641-15-7P 912641-17-9P

912641-19-1P 912641-22-6P 912641-24-8P
912641-27-1P 912641-30-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(enantioselective prepn. of 8-azabicyclo[3.2.1]oct-2-ene derivs. for therapeutic use as monoamine neurotransmitter re-uptake inhibitors)
RN 912641-08-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chlorophenyl)-, (+)- (CA INDEX NAME)

Rotation (+).

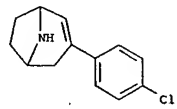


RN 912641-09-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chlorophenyl)-, (+)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 912641-08-8
CMF C13 H14 Cl N

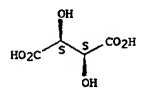
Rotation (+).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.

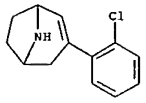


RN 912641-11-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2-chlorophenyl)-, (+)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 912641-10-2
CMF C13 H14 Cl N

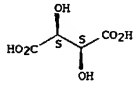
Rotation (+).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.

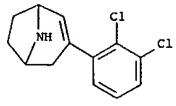


RN 912641-13-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2,3-dichlorophenyl)-, (+)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 912641-12-4
CMF C13 H13 Cl2 N

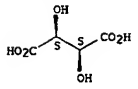
Rotation (+).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.

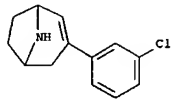


RN 912641-15-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chlorophenyl)-, (+)-,
(2S,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 912641-14-6
CMF C13 H14 Cl N

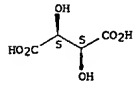
Rotation (+).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.

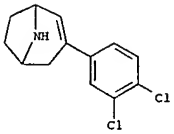


RN 912641-17-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dichlorophenyl)-, (+)-,
(2S,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 912641-16-8
CMF C13 H13 Cl2 N

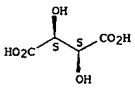
Rotation (+).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.

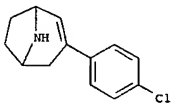


RN 912641-19-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chlorophenyl)-, (-)-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 912641-18-0
CMF C13 H14 Cl N

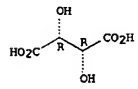
Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

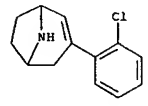


RN 912641-22-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2-chlorophenyl)-, (-)-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 912641-21-5
CMF C13 H14 Cl N

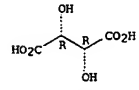
Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

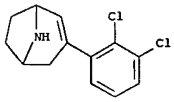


RN 912641-24-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2,3-dichlorophenyl)-, (-)-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 912641-23-7
CMF C13 H13 Cl2 N

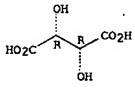
Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

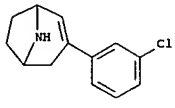


RN 912641-27-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chlorophenyl)-, (-)-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 912641-26-0
CMF C13 H14 Cl N

Rotation (-).

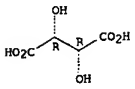


CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

L4 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

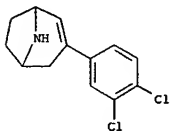


RN 912641-30-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dichlorophenyl)-, (-)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 912641-29-3
CMF C13 H13 C12 N

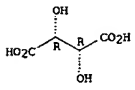
Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



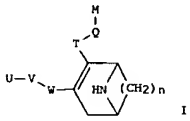
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:916310 CAPLUS
DOCUMENT NUMBER: 145:315016
TITLE: Preparation of bicyclic five-membered heteroaryl derivatives and their use as renin inhibitors
INVENTOR(S): Bezencon, Olivier; Boss, Christoph; Bur, Daniel; Corminboeuf, Olivier; Fischli, Walter; Grisostomi, Corinna; Remen, Lubos; Richard, Sylvia; Sifferlen, Thierry; Weller, Thomas
PATENT ASSIGNEE(S): Actelion Pharmaceuticals Ltd., Switz.
SOURCE: PCT Int. Appl., 64pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006092268	A1	20060908	WO 2006-EP1827	20060228

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2005-EP2189 A 20050302
OTHER SOURCE(S): MARPAT 145:315016
GI



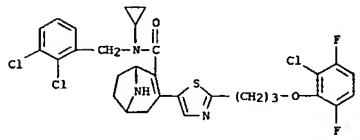
I

AB The invention relates to novel five-membered heteroaryl derivs. I, wherein W represents a five-membered heteroaryl containing two heteroatoms independently selected from O, N and S; V represents -CH2CH2-O-, -CH2CH2CH2-O-, -O-CH2CH2-O-, -O-CH2CH2CH2-O-, -CH2-O-CH2CH2-O-, -O-CH2CH2-O-CH2-, or O-CH2CH2CH2O-CH2-; U is (un)substituted aryl; T represents -CONR1- or -CHCONR1-; Q represents methylene; M represents unsubstituted aryl; or mono- or disubstituted aryl, wherein the substituents are independently selected from the group consisting of alkyl, alkoxy, - OCF3, -CF3, hydroxyalkyl and halogen; R1 represents alkyl or cycloalkyl; and n is the integer 2 or 3; and optically pure enantiomers, mixts. of enantiomers such as a racemates, diastereomers, mixts. of diastereomers, diastereomeric racemates, mixture of diastereomeric racemates, and meso-forms, as well as salts and solvent complexes of such

L4 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
compds., and morphol. forms. and the use thereof as active ingredients in the prepn. of pharmaceutical compns. The invention also concerns related aspects including processes for the prepn. of the compds., pharmaceutical compns. comprising one or more of those compds. and esp. their use as inhibitors of renin. Title compds. were claimed for the prepn. of a pharmaceutical compn. for the treatment or prophylaxis of diseases such as or related to hypertension, congestive heart failure, pulmonary hypertension, renal insufficiency, renal ischemia, renal failure, renal fibrosis, cardiac insufficiency, cardiac hypertrophy, cardiac fibrosis, myocardial ischemia, cardiomyopathy, glomerulonephritis, renal colic, complications resulting from diabetes such as nephropathy, vasculopathy and neuropathy, glaucoma, elevated intra-ocular pressure, atherosclerosis, restenosis post angioplasty, complications following vascular or cardiac surgery, erectile dysfunction, hyperaldosteronism, lung fibrosis, scleroderma, anxiety, cognitive disorders, complications of treatments with immunosuppressive agents, and other diseases known to be related to the renin-angiotensin system. Title compds. exhibit in vitro human renin inhibition with IC50 values between 0.1 nM to 300 nM, esp. between 1 nM to 30 nM. Thus, (rac)-(1R*,5S*)-3-[2-[2-(2,6-dichlorophenoxy)ethoxymethyl]thiazol-5-yl]-9-azabicyclo[3.3.1]non-2-ene-2-carboxylic acid cyclopropyl(2,3-dichlorobenzyl)amide was prepd. and tested in vitro as renin inhibitor (IC50 = 11 nM).

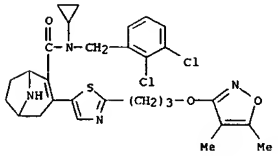
IT 909396-20-9P 909396-21-0P 909396-22-1P
909396-23-2P 909396-24-3P 909396-25-4P
909396-26-5P 909396-27-6P 909396-28-7P
909396-29-8P 909396-30-1P 909396-31-2P
909396-32-3P 909396-33-4P 909396-34-5P
909396-39-0P 909396-40-3P 909396-41-4P
909396-42-5P 909396-43-6P 909396-44-7P
909396-72-1P 909396-73-2P 909396-74-3P
909396-75-4P 909396-76-5P 909396-77-6P
909396-78-7P 909396-79-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bicyclic five-membered heteroaryl derivs. and their use as renin inhibitors)

RN 909396-20-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[2-[3-(2-chloro-3,6-difluorophenoxy)propyl]-5-thiazolyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)

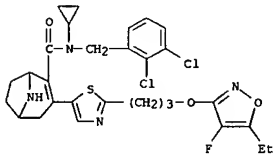


RN 909396-21-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-3-[2-[3-[(4,5-dimethyl-3-isoxazolyl)oxy]propyl]-5-thiazolyl]- (CA INDEX NAME)

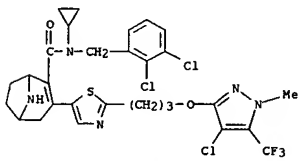
L4 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



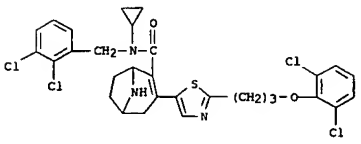
RN 909396-22-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]-3-[2-[3-[(5-ethyl-4-fluoro-3-isoxazolyl)oxy]propyl]-5-thiazolyl]- (CA INDEX NAME)



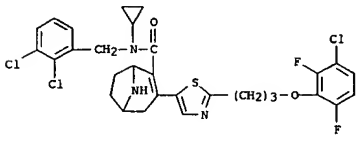
RN 909396-23-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[2-[3-[[4-chloro-1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl]oxy]propyl]-5-thiazolyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



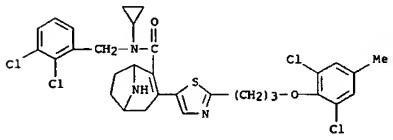
RN 909396-24-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[3-(2,6-dichlorophenoxy)propyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



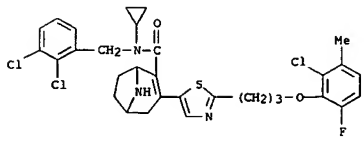
RN 909396-25-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[2-[3-(3-chloro-2,6-difluorophenoxy)propyl]-5-thiazolyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



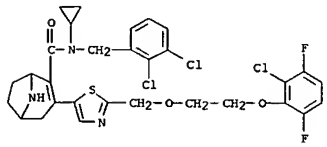
RN 909396-26-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[3-(2,6-dichloro-4-methylphenoxy)propyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



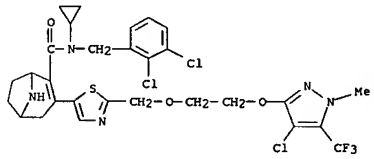
RN 909396-27-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[2-[3-(2-chloro-6-fluoro-3-methylphenoxy)propyl]-5-thiazolyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



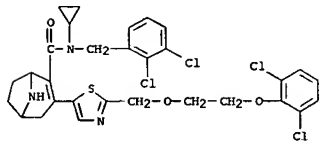
RN 909396-28-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[2-[[2-(2-chloro-3,6-difluorophenoxy)ethoxy]methyl]-5-thiazolyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



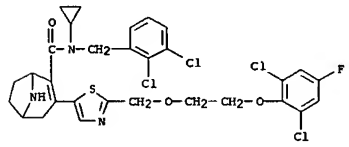
RN 909396-29-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[2-[[2-[[4-chloro-1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-yl]oxy]ethoxy]methyl]-5-thiazolyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



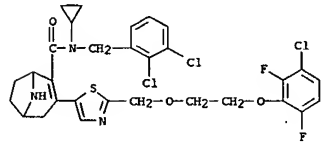
RN 909396-30-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[[2-(2,6-dichlorophenoxy)ethoxy]methyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



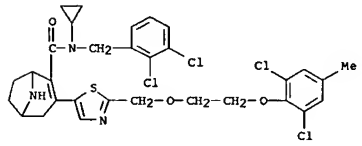
RN 909396-31-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[[2-(2,6-dichloro-4-fluorophenoxy)ethoxy]methyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



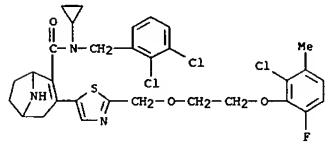
RN 909396-32-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[2-[[2-(3-chloro-2,6-difluorophenoxy)ethoxy]methyl]-5-thiazolyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



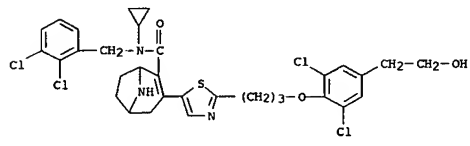
RN 909396-33-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[[2-(2,6-dichloro-4-methylphenoxy)ethoxy]methyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



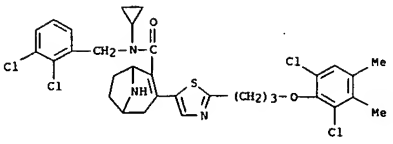
RN 909396-34-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[2-[[2-(2-chloro-6-fluoro-3-methylphenoxy)ethoxy]methyl]-5-thiazolyl]-N-cyclopropyl-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



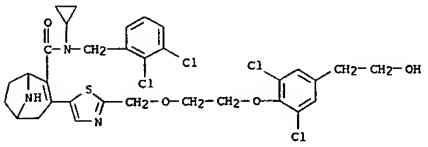
RN 909396-39-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[3-[2,6-dichloro-4-(2-hydroxyethyl)phenoxy]propyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



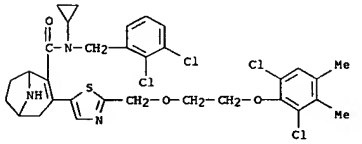
RN 909396-40-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[3-(2,6-dichloro-3,4-dimethylphenoxy)propyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



RN 909396-41-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[[2-[2,6-dichloro-4-(2-hydroxyethyl)phenoxy]ethoxy]methyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)

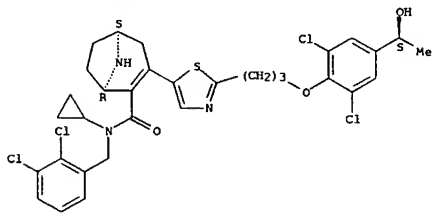


RN 909396-42-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[[2-(2,6-dichloro-3,4-dimethylphenoxy)ethoxy]methyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]- (CA INDEX NAME)



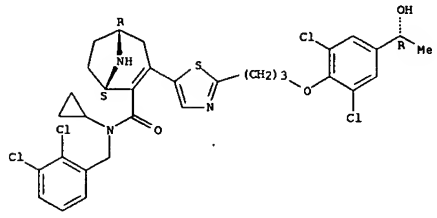
RN 909396-43-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[2-[2-(2-chloro-3,6-difluorophenoxy)ethoxy]-5-thiazolyl]-N-cyclopropyl-N-[(3-methoxy-2-methylphenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



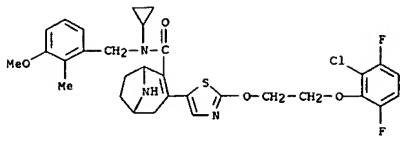
RN 909396-74-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[3-[2,6-dichloro-4-[(1R)-1-hydroxyethyl]phenoxy]propyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]-, (1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.

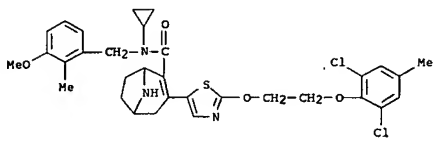


RN 909396-75-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[3-[2,6-dichloro-4-[(1S)-1-hydroxyethyl]phenoxy]propyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]-, (1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.

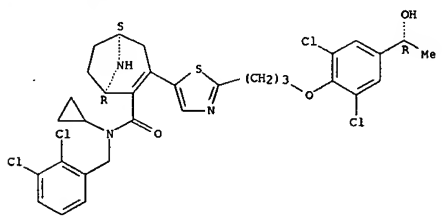


RN 909396-44-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[2-(2,6-dichloro-4-methylphenoxy)ethoxy]-5-thiazolyl]-N-[(3-methoxy-2-methylphenyl)methyl]- (CA INDEX NAME)

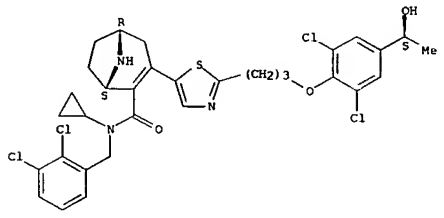


RN 909396-72-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[3-[2,6-dichloro-4-[(1R)-1-hydroxyethyl]phenoxy]propyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]-, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.

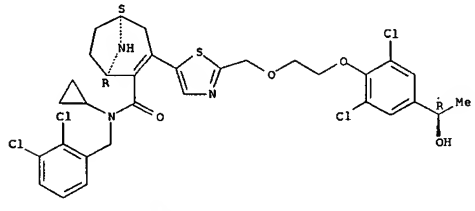


RN 909396-73-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[3-[2,6-dichloro-4-[(1S)-1-hydroxyethyl]phenoxy]propyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]-, (1R,5S)- (CA INDEX NAME)



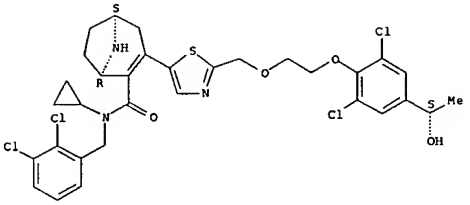
RN 909396-76-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[[2-[2,6-dichloro-4-[(1R)-1-hydroxyethyl]phenoxy]ethoxy]methyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]-, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.



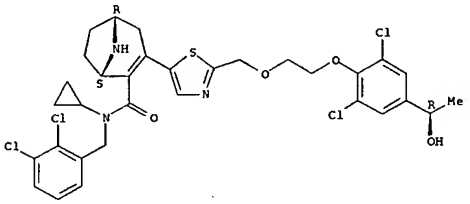
RN 909396-77-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[[2-[2,6-dichloro-4-[(1S)-1-hydroxyethyl]phenoxy]ethoxy]methyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]-, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 909396-78-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[[2-[2,6-dichloro-4-[(1R)-1-hydroxyethyl]phenoxy]ethoxy]methyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]-, (1S,5R)- (CA INDEX NAME)

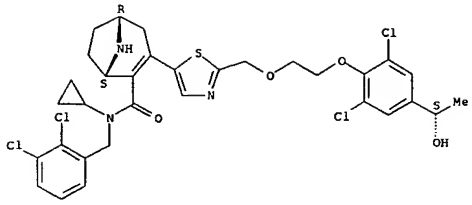
Absolute stereochemistry.



RN 909396-79-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[2-[[2-[2,6-dichloro-4-[(1S)-1-hydroxyethyl]phenoxy]ethoxy]methyl]-5-thiazolyl]-N-[(2,3-dichlorophenyl)methyl]-, (1S,5R)- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

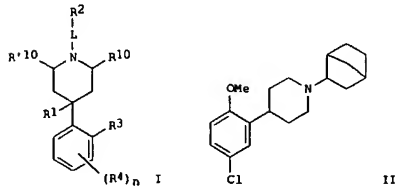
L4 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:515972 CAPLUS
DOCUMENT NUMBER: 145:27871
TITLE: N-Substituted 4-arylpiperidine derivatives as modulators of muscarinic receptors and their preparation, pharmaceutical composition and use for treatment of muscarinic receptor-mediated diseases
INVENTOR(S): Hurley, Dennis J.; Bergeron, Daniele M.; Drutu, Ioana; Garcia-Guzman Blanco, Miguel; Makings, Lewis R.; Nakatani, Akiko; Raffai, Gabriel; Silina, Alina
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006058294	A2	20060601	WO 2005-US42931	20051129
WO 2006058294	A3	20070118		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006287303	A1	20061221	US 2005-288938	20051129
EP 1817032	A2	20070815	EP 2005-852296	20051129
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.: US 2004-631560P P 20041129
WO 2005-US42931 W 20051129

OTHER SOURCE(S): MARPAT 145:27871
GI



I

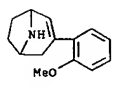
II

L4 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB The invention relates to compound of formula I and their use as modulators of muscarinic receptors. The invention also provides compns. comprising such modulators, and methods therewith for treating muscarinic receptor mediated diseases. Compds. of formula I wherein R1 is ZAR5; R2 is (un)substituted mono(hetero)cycloalkyl, (un)substituted bicyclic cycloalkyl, (un)substituted bridge bicyclic heterocycloalkyl, or (un)substituted adamantyl; R3 is ZCR8; R4 is ZDR9; ZA, ZC and ZD are independently a bond, (un)substituted (un)branched C1-6 aliphatic chain, etc.; R5, R8 and R9 are independently H, (un)substituted C1-8 alkyl, (un)substituted (hetero)cycloalkyl, (un)substituted (hetero)aryl, halo, OH, NH2, NO2, CN or OCF3; L is a bond or CH2; R10 and R'10 are independently H or C1-4 aliphatic; n is 0-4; and their pharmaceutically acceptable salts are claimed in this invention. Example compound II was prepared by methylation of 2-bromo-4-chlorophenol; the resulting anisole underwent addition to 1-benzyl-4-piperidinone to give 1-benzyl-4-(4-chloro-2-methoxyphenyl)-4-piperidinol, which underwent elimination, reduction, and debenzylation to give 4-(4-chloro-2-methoxyphenyl)piperidine, which reacted with norcamphor to give example compound II. All the invention compds. were evaluated for their activities and efficacies for modulating M1, M2, M3, and M3 receptors. The compds. were found to modulate M1 and/or M4 muscarinic receptors selectively over the other receptor types.

IT 888966-00-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of N-substituted arylpiperidine derivs. as modulators of muscarinic receptors)

RN 888966-00-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(2-methoxyphenyl)- (CA INDEX NAME)

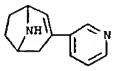


L4 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:427357 CAPLUS
DOCUMENT NUMBER: 145:124531
TITLE: New Ligands with Affinity for the α4β2 Subtype of Nicotinic Acetylcholine Receptors. Synthesis, Receptor Binding, and 3D-QSAR Modeling
AUTHOR(S): Audouze, Karine; Oestergaard Nielsen, Elsebet; Olsen, Gunnar M.; Ahring, Philip; Jorgensen, Tino Dyhring; Peters, Dan; Liljefors, Tommy; Balle, Thomas
CORPORATE SOURCE: NeuroSearch A/S, Ballerup, DK-2750, Den.
SOURCE: Journal of Medicinal Chemistry (2006), 49(11), 3159-3171
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:124531

AB A new series of piperazines, diazepanes, diazocanes, diazabicyclononanes, and diazabicyclodecanes with affinity for the α4β2 subtype of nicotinic acetylcholine receptors were synthesized on the basis of results from a previous computational study. A predictive 3D-QSAR model was developed using the GRID/GOLPE approach (R2 = 0.94, Q2 = 0.83, SDEP = 0.34). The SAR was interpreted in terms of contour maps of the PLS coeffs. and in terms of a homol. model of the α4β2 subtype of the nicotinic acetylcholine receptors. The results reveal that hydrogen bonding from both hydrogens on the protonated amine and from the pyridine nitrogen to a water mol. as well as van der Waals interactions between the substituent bearing the protonated amine and the receptor is of importance for ligand affinity. The combination of 3D-QSAR and homol. modeling proved successful for the interpretation of structure-affinity relationships as well as the validation of the individual modeling approaches.

IT 216853-22-4
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation, receptor binding, and 3D-QSAR modeling of new ligands with affinity for the α4β2 subtype of nicotinic acetylcholine receptors)

RN 216853-22-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-pyridinyl)- (CA INDEX NAME)

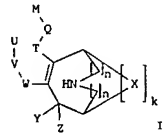


REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:523457 CAPLUS
DOCUMENT NUMBER: 143:59835
TITLE: Preparation of azabicyclooctene derivatives and related compounds as renin inhibitors
INVENTOR(S): Bezencon, Olivier; Sifferlen, Thierry; Bur, Daniel; Fischli, Walter; Weller, Thomas; Remen, Lubos; Richard-Bildstein, Sylvia
PATENT ASSIGNEE(S): Actelion Pharmaceuticals Ltd., Switz.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005054244	A2	20050616	WO 2004-EP13579	20041130
WO 2005054244	A3	20050804		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004295092	A1	20050616	AU 2004-295092	20041130
CA 2547551	A1	20050616	CA 2004-2547551	20041130
EP 1692132	A2	20060823	EP 2004-803362	20041130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1890239	A	20070103	CN 2004-80035893	20041130
JP 2007513107	T	20070524	JP 2006-541865	20041130
US 2007135406	A1	20070614	US 2006-581824	20060602
IN 2006CN02463	A	20070608	IN 2006-CN2463	20060705
PRIORITY APPLN. INFO.:			WO 2003-EP313771 A	20031205
			WO 2004-EP13579 W	20041130

OTHER SOURCE(S): CASREACT 143:59835; MARPAT 143:59835
GI



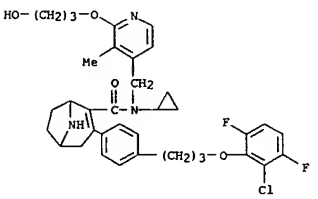
AB Bicyclic derivs. (I) [wherein Y, Z = H, F, Me; or Y and Z may together

L4 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
form a cyclopropyl ring; X = (CH2)mN(L)(CH2)n, CH2CH(K)CH2, CH2CH2, CH2OCH2, CH2SCH2, CH2SOCH2, CH2SO2CH2, CON(L)CO, etc.; W = six-membered, non benzofused, Ph or heteroaryl ring, substituted by V in position 3 or 4; V = a bond, (CH2)r, A-(CH2)s, CH2-A-(CH2)t, (CH2)s-A, (CH2)2-A-(CH2)u, A-(CH2)v-B, (CH2)3-A-CH2, etc.; A, B = O, S, SO, SO2; U = aryl, heteroaryl; T = CONR1, (CH2)pOCO, (CH2)pN(R1)CO, etc.; Q = lower alkylene or alkenylene; M = aryl-O(CH2)vR5, heteroaryl-O(CH2)vR5, aryl-O(CH2)vO(CH2)wR5, heteroaryl-(CH2)vO(CH2)wR5, aryl-OCH2CH(R7)CH2R5, etc.; L = R3, COR3, CO2R3, CONR2R3, SO2R3, SO2NR2R3, etc.; K = H, CH2OR3,CH2NR2COR3, CH2NR2SO2R3, CO2R3, CH2OCONR2R3, etc; R1 = H, lower alkyl, alkenyl, or alkynyl, cycloalkyl, aryl, etc.; R2, R2' = H, lower alkyl or alkenyl, cycloalkyl, cycloalkyl-lower alkyl; R3 = H, lower alkyl or alkenyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl-lower alkyl, aryl-lower alkyl, etc. R5 = OH, lower alkoxy, OCOR2, CO2R2, NR2R2', OCONR2R2', NCONR2R2', cyano, -CONR2R2', SO3H, etc.; R6 = H, (un)substituted lower alkyl or alkoxy; R7 = OH, OR2, OCOR2, OCOOR2; k, m, n = 0, 1; p, t, v = 1-4; r = 1-6; s = 1-5; u = 1-3; w = 1,2] and optically pure enantiomers, mixts. of enantiomers, or pharmaceutically acceptable salts are prepd. These compds. are inhibitors of renin and useful for the treatment or prophylaxis of diseases known to be related to the renin-angiotensin system. The diseases include hypertension, congestive heart failure, pulmonary hypertension, renal insufficiency, renal ischemia, renal failure, renal fibrosis, cardiac insufficiency, cardiac hypertrophy, cardiac fibrosis, myocardial ischemia, cardiomyopathy, glomerulonephritis, renal colic, complications resulting from diabetes such as nephropathy, vasculopathy and neuropathy, glaucoma, elevated intraocular pressure, atherosclerosis, restenosis post angioplasty, complications following vascular or cardiac surgery, erectile dysfunction, hyperaldosteronism, lung fibrosis, scleroderma, anxiety, cognitive disorders, complications of treatments with immunosuppressive agents, and other diseases known to be related to the renin-angiotensin system. For example, 3-[4-[3-(2-Chloro-3,6-difluorophenoxy)propyl]phenyl]-8-azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid N-cyclopropyl-N-[2-(3-methoxypropoxy)-3-methylpyridin-4-ylmethyl]amide showed IC50 of 0.79 nM against human recombinant renin.

IT 851377-75-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of azabicyclooctene derivs. and related compds.
as renin inhibitors treatment or prophylaxis of diseases related to renin-angiotensin system)

RN 851377-75-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[[2-(3-hydroxypropoxy)-3-methyl-4-pyridinyl]methyl]- (CA INDEX NAME)

L4 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 854019-55-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azabicyclooctene derivs. and related compds. as renin inhibitors treatment or prophylaxis of diseases related to renin-angiotensin system)

RN 854019-55-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[[2-(3-methoxypropoxy)-3-methyl-4-pyridinyl]methyl]- (CA INDEX NAME)

L4 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:395318 CAPLUS
DOCUMENT NUMBER: 142:463606
TITLE: Preparation of azabicycloalkenes as renin inhibitors
INVENTOR(S): Bezencon, Olivier; Sifferlen, Thierry; Bur, Daniel; Fischli, Walter; Weller, Thomas; Remen, Lubos; Richard-Bildstein, Sylvia
PATENT ASSIGNEE(S): Actelion Pharmaceuticals Ltd., Switz.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005040173	A1	20050506	WO 2004-EP11704	20041018
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004283854	A1	20050506	AU 2004-283854	20041018
CA 2540817	A1	20050506	CA 2004-2540817	20041018
EP 1680427	A1	20060719	EP 2004-765982	20041018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1930170	A	20070314	CN 2004-80030679	20041018
JP 2007509099	T	20070412	JP 2006-536020	20041018
US 2007135405	A1	20070614	US 2006-576904	20060421
IN 2006CN01802	A	20070706	IN 2006-CN1802	20060523
PRIORITY APPLN. INFO.:			WO 2003-EP11704 A	20031023
			WO 2004-EP11704 W	20041018

OTHER SOURCE(S): MARPAT 142:463606
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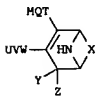
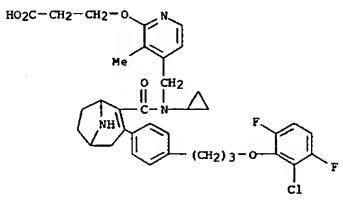


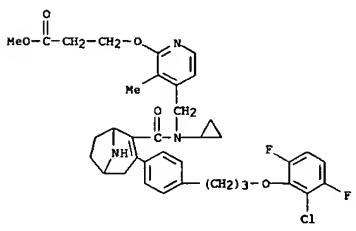
AB Title compds. [I; Y, Z = H, F, Me; YZ = atoms to form a cyclopropyl ring; X = CH2CHXCH2, CH2CH2, CH2OCH2; CH2SCH2, CH2SOCH2, CH2SO2CH2, CONLCHR6; W = Ph, heteroaryl; V = bond, (CH2)r, A(CH2)s, OCHMeCH2O, etc.; A = O, S, SO, SO2; U = aryl, heteroaryl; T = CONR1, (CH2)pO2C, CO2, etc.; Q = alkylene, alkenylene; M = ArO(CH2)vR5, ArOCH2CH2O(CH2)wR5; Ar = aryl, heteroaryl; X = H, CH2OR3, CH2NR2R3, etc.; L = R3, COR3, CO2R3, CONR2R3, SO2R3, SO2NR2R3; R1 = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl,

L4 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

yl]carbonyl]cyclopropylamino]methyl]-3-methyl-2-pyridinyl]oxy]- (CA INDEX NAME)



RN 851377-78-1 CAPLUS
CN Propanoic acid, 3-[[4-[[[[3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-8-azabicyclo[3.2.1]oct-2-en-2-yl]carbonyl]cyclopropylamino]methyl]-3-methyl-2-pyridinyl]oxy]-, methyl ester (CA INDEX NAME)



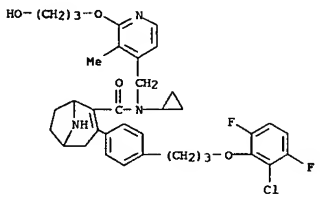
RN 851377-79-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-[[2-(3-amino-3-oxopropoxy)-3-methyl-4-pyridinyl]methyl]-3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl- (CA INDEX NAME)

L4 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

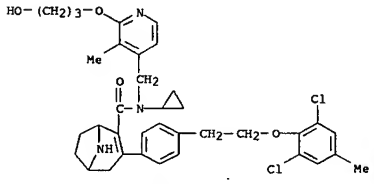
cycloalkylalkyl; R2 = H, alkyl, alkenyl, cycloalkyl, cycloalkylalkyl; R3 = H, alkyl, alkenyl, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, heterocyclyl, etc.; R5 = OH, O2CR2, CO2R2, cyano, SO3H, morpholinocarbonyl, etc.; R6 = H, (substituted) alkyl, alkoxy; p = 1-4; r = 1-6; v = 2-4; w = 1, 2], were prepd. Thus, rac-(1R*,5S*)-3-[4-[2-(2,6-dichloro-4-methylphenoxy)ethoxy]phenyl]-8-azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid cyclopropyl[2-(3-hydroxypropoxy)-3-methylpyridin-4-ylmethyl]amide (multistep prepn. given) inhibited human recombinant renin with IC50 = 0.18 nM.

IT 851377-75-8P 851377-76-9P 851377-77-0P
851377-78-1P 851377-79-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of azabicycloalkenes as renin inhibitors)

RN 851377-75-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, 3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-N-cyclopropyl-N-[[2-(3-hydroxypropoxy)-3-methyl-4-pyridinyl]methyl]- (CA INDEX NAME)

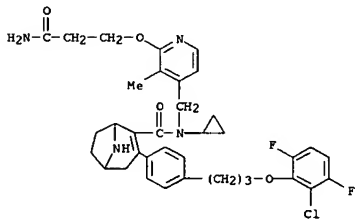


RN 851377-76-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxamide, N-cyclopropyl-3-[4-[2-(2,6-dichloro-4-methylphenoxy)ethyl]phenyl]-N-[[2-(3-hydroxypropoxy)-3-methyl-4-pyridinyl]methyl]- (CA INDEX NAME)



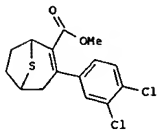
RN 851377-77-0 CAPLUS
CN Propanoic acid, 3-[[4-[[[[3-[4-[3-(2-chloro-3,6-difluorophenoxy)propyl]phenyl]-8-azabicyclo[3.2.1]oct-2-en-2-

L4 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:967769 CAPLUS
DOCUMENT NUMBER: 142:113868
TITLE: Synthesis of 8-thiabicyclo[3.2.1]oct-2-enes and their binding affinity for the dopamine and serotonin transporters
AUTHOR(S): Meltzer, Peter C.; Pham-Huu, Duy-Phong; Madras, Bertha K.
CORPORATE SOURCE: Organix Inc., Woburn, MA, 01801, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(24), 6007-6010
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:113868
GI



I

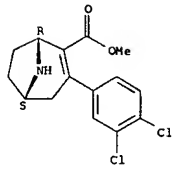
AB The reinforcing and stimulant properties of cocaine have been primarily associated with its propensity to bind to monoamine transport systems, in particular the dopamine transporter. Inhibition of the dopamine transporter then leads to an increase of synaptic dopamine with substantial pharmacol. consequences. The search for medications for cocaine abuse has had a particular focus on tropane analogs of cocaine, and the interchange of nitrogen for oxygen in this class has led to potent and selective inhibitors of monoamine transport. Herein it is reported that 8-thiatrop-2-enes are highly potent and quite selective inhibitors of the dopamine transporter. 3-(3,4-Dichlorophenyl)-8-oxabicyclo[3.2.1]oct-2-ene-2-carboxylic acid Me ester (I) is particularly potent (IC50 = 4.5 nM) and selective (800-fold) with respect to inhibition of the serotonin transporter.

IT 306740-86-3
RL: PAC (Pharmacological activity); BIOL (Biological study)
(comparison of (aryl)-8-thiabicyclo[3.2.1]oct-2-ene-2-carboxylic acid ester with (aryl)-8-azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid ester (O-1109) for binding affinity for dopamine and serotonin transporters)

RN 306740-86-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-(3,4-dichlorophenyl)-, methyl ester, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



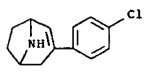
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:880487 CAPLUS
DOCUMENT NUMBER: 142:32443
TITLE: Haloperidol: towards further understanding of the structural contributions of its pharmacophoric elements at D2-like receptors
AUTHOR(S): Sikazwe, Donald M. N.; Li, Shouming; Mardenborough, Leroy; Cody, Vivian; Roth, Brian L.; Ablordeppey, Seth Y.
CORPORATE SOURCE: College of Pharmacy and Pharmaceutical Sciences, Florida A & M University, Tallahassee, FL, 32307, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(23), 5739-5742
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:32443

AB An attempt to understand the pharmacophore-relevant position of the alc. moiety in haloperidol and the contributions of other pharmacophoric elements led to the resynthesis of its tropane analog (compound 2). An anal. of the binding data suggests that haloperidol binds to the DA receptors with the OH group in the axial position and the OH group, while not essential for binding, enhances binding especially at the D2 receptor. It also became clear that shortening the butyrophenone chain not only reduces binding affinity at the DA receptors but eliminates subtype selectivity.

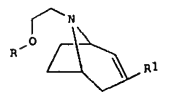
IT 189746-53-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pharmacophoric elements of haloperidol impacting activity at D2-like receptors)

RN 189746-53-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chlorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:791925 CAPLUS
DOCUMENT NUMBER: 141:411119
TITLE: Novel aryloxy-8-azabicyclo[3.2.1]oct-3-enes with 5-HT transporter and 5-HT1A affinity
AUTHOR(S): Gilbert, Adam M.; Coleman, Thomas; Kodah, Jason; Mewshaw, Richard E.; Scerni, Rosemary; Schechter, Lee E.; Smith, Deborah L.; Andree, Terrance H.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Pearl River, NY, 10965-1215, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(21), 5281-5284
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:411119
GI



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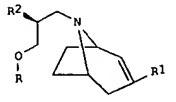


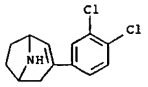
II

AB Joining aryl 8-azabicyclo[3.2.1]oct-3-enes with aryloxyethanes and aryloxypropanes produces novel series of compds. I [R = 4-indanyl, 5-, 8-quinolinyl, 4-indolyl, 1-methyl-4-indolyl, R1 = 2-naphthyl; R = 5-quinolinyl, R1 = 2-indolyl; R = 4-indolyl, R1 = 2-naphthyl, 3-benzo[b]thiophenyl, C6H3-3,4-Cl2, 3-indolyl; R = 8-benzodioxanyl, R1 = 3-indolyl] and II [R = 4-indolyl, R1 = 3-indolyl, 2-naphthyl, C6H3-3,4-Cl2, R2 = H; R = 4-indolyl, R1 = 2-naphthyl, C6H4-3,4-Cl2, R2 = OH] with potent 5-HT-T affinity and moderately potent 5-HT1A affinity. Moreover, several of these compds. possess functional 5-HT1A antagonism. Optimal compds. are, 4-indolyloxyethane I (R = 4-indolyl, R1 = 3-indolyl), and 4-indolyloxypropanes II (R = 4-indolyl, R1 = 2-naphthyl, R = C6H3-3,4-Cl2, R2 = OH), which possess potent 5-HT-T affinity (5-HT-T Ki: I (R = 4-indolyl, R1 = 3-indolyl): 1.2 nM, II (R = 4-indolyl, R1 = 2-naphthyl, R2 = OH): 0.54 nM, 27: 0.38 nM) and good 5-HT1A affinity/antagonism (5-HT1A Ki, [35S]GTPγS: Emax (%): 111.1 nM, 0%; 173.2 nM, 0%; 107 nM, 0%, resp.).

IT 189746-56-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(aryloxy-8-azabicyclo[3.2.1]oct-3-enes with 5-HT transporter and 5-HT1A affinity)

RN 189746-56-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dichlorophenyl)- (CA INDEX NAME)

L4 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

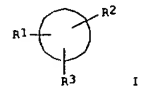
ACCESSION NUMBER: 2004:220079 CAPLUS
DOCUMENT NUMBER: 140:253575
TITLE: Preparation of heteroaryl-substituted pyrrole derivatives that inhibit production of TNFα
INVENTOR(S): Kimura, Tomio; Aoki, Kazumasa; Nakao, Akira; Ushiyama, Shigeru; Shimozato, Takaichi; Ohkawa, Nobuyuki; Nagasaki, Takayoshi; Yamazaki, Takanori
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: U.S. Pat. Appl. Publ., 244 pp., Cont.-in-part of U.S. Ser. No. 317,748, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004054173	A1	20040318	US 2003-354648	20030130
US 7122666	B2	20061017		
RU 2198170	C2	20030210	RU 2000-119431	20000720
ZA 2000003705	A	20010205	ZA 2000-3705	20000721
JP 2002284783	A	20021003	JP 2002-12247	20020122
US 2005283006	A1	20051222	US 2003-411061	20030410
ZA 2003005585	A	20041026	ZA 2003-5585	20030718
US 2006128756	A1	20060615	US 2006-339390	20060125

PRIORITY APPLN. INFO.:

JP 1999-205491	A	19990721
JP 1999-369678	A	19991227
US 2000-619898	B3	20000719
JP 2001-13817	A	20010122
US 2001-275005P	P	20010312
US 2002-54630	B2	20020122
US 2002-99176	B1	20020314
US 2002-317748	B2	20021212
US 2003-354648	A1	20030130

OTHER SOURCE(S): MARPAT 140:253575
GI



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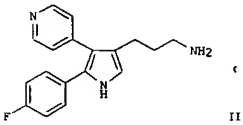


II

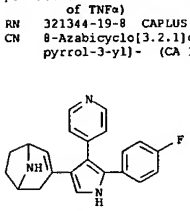
L4 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB Title compds. I [A = pyrrole; R1 = (un)substituted Ph, naphthyl, etc.; R2 = pyridinyl, pyrimidinyl, etc.; R3 = heterocyclyl] are prepared For instance, α-(p-toluenesulfonyloxy)-4-fluorobenzylisonitrile is reacted with 3-(4-pyridyl)acrylate (THF, n-BuLi, LiBr, -45°) to give 4-(ethoxycarbonyl)-2-(4-fluorophenyl)-3-(pyridin-4-yl)-1H-pyrrole. This Et ester is reduced (THF/PhMe, DIBAL), oxidized to the 4-formyl derivative (DMSO, MnO2, 50°), condensed with diethylphosphonoacetonitrile (THF, NaH). This adduct was reduced (THF/MeOH, H2-Pd/C) and reduced (THF, LAH) to give II. Compds. of the invention inhibit production of TNFα and IL-1β. I are useful for the treatment of inflammation.

IT 321344-19-8P, 4-(8-Azabicyclo[3.2.1]oct-2-en-3-yl)-2-(4-fluorophenyl)-3-(pyridin-4-yl)-1H-pyrrole
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heteroaryl-substituted pyrrole derivs. that inhibit production of TNFα)

RN 321344-19-8 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrrol-3-yl]- (CA INDEX NAME)



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:214127 CAPLUS
DOCUMENT NUMBER: 141:7313
TITLE: Synthesis and nicotinic acetylcholine receptor binding affinities of 2- and 3-isoxazolyl-8-azabicyclo[3.2.1]octanes
AUTHOR(S): Cheng, Jie; Izenwasser, Sari; Zhang, Chunming; Zhang, Suhong; Wade, Dean; Trudell, Mark L.
CORPORATE SOURCE: Department of Chemistry, University of New Orleans, New Orleans, LA, 70148, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(7), 1775-1778
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:7313

AB A series of epiboxidine homologs, 2- and 3-isoxazole substituted 8-azabicyclo[3.2.1]octane derivs., were synthesized and evaluated as potential ligands for neuronal nicotinic acetylcholine receptors in [3H]cytisine labeled rat brain. 2β-(5-Methyl-3-isoxazolyl)-8-azabicyclo[3.2.1]octane (Ki=3 nM) was the most potent compound of the series with a binding affinity twice that of nicotine. 3β-(3-Methyl-5-isoxazolyl)-8-azabicyclo[3.2.1]octane (Ki=148 nM) exhibited moderate affinity while the corresponding 2α- and 3α-isomers exhibited micromolar binding affinity.

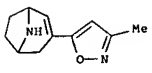
IT 693235-58-4
RL: PAC (Pharmacological activity); BIOL (Biological study)
(preparation and nicotinic acetylcholine receptor binding affinities of 2- and 3-isoxazolyl-8-azabicyclo[3.2.1]octanes)

RN 693235-58-4 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-methyl-5-isoxazolyl)-, ethanedioate (1:1) (CA INDEX NAME)

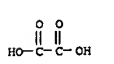
CM 1

CRN 693235-57-3
CMF C11 H14 N2 O



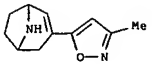
CM 2

CRN 144-62-7
CMF C2 H2 O4



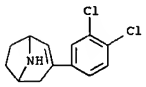
IT 693235-57-3P

L4 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and nicotinic acetylcholine receptor binding affinities of 2- and 3-isoxazolyl-8-azabicyclo[3.2.1]octanes)
RN 693235-57-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-methyl-5-isoxazolyl)- (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

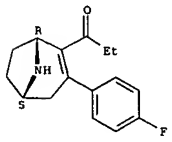
L4 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:1002001 CAPLUS
DOCUMENT NUMBER: 140:314412
TITLE: Modulation of selective serotonin reuptake inhibitor and 5-HT1A antagonist activity in 8-aza-bicyclo[3.2.1]octane derivatives of 2,3-dihydro-1,4-benzodioxane
AUTHOR(S): Gilbert, Adam M.; Stack, Gary P.; Nilakantan, Ramaswamy; Kodah, Jason; Tran, Megan; Scerni, Rosemary; Shi, Xiaojie; Smith, Deborah L.; Andree, Terrance H.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Pearl River, NY, 10945, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(2), 515-518
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:314412
AB 2,3-Dihydro-1,4-benzodioxanes with acyl 8-aza-bicyclo[3.2.1]oct-3-ene attachments produce compds. with potent 5-HT-T affinity, and weak 5-HT1A affinity and α1 affinity. This compares with 2,3-dihydro-1,4-benzodioxanes containing 8-aza-bicyclo[3.2.1] octan-3-ol attachments which possess potent 5-HT1A affinity, moderate to good selectivity over α1 and little 5-HT-T affinity. A 3-benzothiophene analog was synthesized which possesses potent 5-HT1A affinity and especially good selectivity over both α1 and 5-HT-T.
IT 189746-56-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(modulation of selective serotonin reuptake inhibitor and 5-HT1A antagonist activity in 8-aza-bicyclo[3.2.1]octane derivs. of 2,3-dihydro-1,4-benzodioxane)
RN 189746-56-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dichlorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:509104 CAPLUS
DOCUMENT NUMBER: 139:210118
TITLE: A Second-Generation 99mTechnetium Single Photon Emission Computed Tomography Agent That Provides in Vivo Images of the Dopamine Transporter in Primate Brain
AUTHOR(S): Meltzer, Peter C.; Blundell, Paul; Zona, Thomas; Yang, Lihua; Huang, Hong; Bonab, Ali A.; Livni, Eli; Fischman, Alan; Madras, Bertha K.
CORPORATE SOURCE: Organix Inc., Woburn, MA, 01801, USA
SOURCE: Journal of Medicinal Chemistry (2003), 46(16), 3483-3496
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The dopamine transporter (DAT), located presynaptically on dopamine neurons, provides a marker for Parkinson's disease (Pd) and attention deficit hyperactivity disorder (ADHD). In ADHD, DAT d. levels are elevated, while in Pd these levels are depleted. The depletion of DAT levels also corresponds with the loss of dopamine. We now describe the design, synthesis, biol., and SPECT imaging in nonhuman primates of second-generation 99mtechnetium-based tropane ligands that bind potently and selectively to the DAT. We demonstrate that improved selectivity and biol. stability allows sufficient agent to enter the brain and label the DAT in vivo to provide a quant. measure of DAT d. in nonhuman primates. We introduce FLUORATEC (N-[(2-((3'-N'-propyl-(1'R)-3''α-(4-fluorophenyl)tropane-2''β-1-propanoyl)(2-mercaptoethyl)amino)acetyl)-2-aminoethanethiolato]technetium(V) oxide), a DAT imaging agent that has emerged from these studies and is now in phase 1 clin. trials in the U.S.
IT 588728-76-1P 588728-77-2P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(second-generation 99Tc SPECT agent: preparation and imaging brain dopamine transporter)
RN 588728-76-1 CAPLUS
CN 1-Propanone, 1-[(1R,5S)-3-(4-fluorophenyl)-8-azabicyclo[3.2.1]oct-2-en-2-yl]- (CA INDEX NAME)

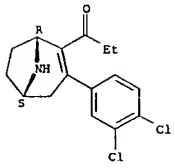
Absolute stereochemistry.



RN 588728-77-2 CAPLUS
CN 1-Propanone, 1-[(1R,5S)-3-(3,4-dichlorophenyl)-8-azabicyclo[3.2.1]oct-2-en-2-yl]- (CA INDEX NAME)

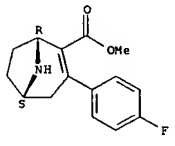
Absolute stereochemistry.

L4 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



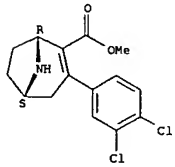
IT 306740-85-2P 306740-86-3P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(second-generation 99Tc SPECT agent: preparation and imaging brain dopamine transporter)
RN 306740-85-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-(4-fluorophenyl)-, methyl ester, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 306740-86-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-(3,4-dichlorophenyl)-, methyl ester, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

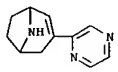
L4 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:322576 CAPLUS
DOCUMENT NUMBER: 139:30178
TITLE: 3D QSAR analyses-guided rational design of novel ligands for the (α4)2(β2)3 nicotinic acetylcholine receptor
AUTHOR(S): Gohlke, Holger; Schwarz, Simone; Guendisch, Daniela; Tilotta, Maria Cristina; Weber, Alexander; Wegge, Thomas; Seitz, Gunther
CORPORATE SOURCE: Institut fuer Pharmazeutische Chemie, Philipps-Universitaet Marburg, Marburg, D-35032, Germany
SOURCE: Journal of Medicinal Chemistry (2003), 46(11), 2031-2048
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:30178

AB Three-dimensional quant. structure-activity relation methods, the comparative mol. field anal. (CoMFA) and the comparative mol. similarity indexes anal. (CoMSIA), were applied using a training set of 45 ligands of the (α4)2(β2)3 nicotinic acetylcholine receptor (nAChR). All compds. are related to (-)-epibatidine, (-)-cytisine, (+)-anatoxin-a, and (-)-ferruginine, and addnl., novel diazabicyclo[4.2.1]nonane- and quinuclidin-2-ene-based structures were included. Their biol. data have been determined by utilizing the same exptl. protocol. Statistically reliable models of good predictive power (CoMFA r2 = 0.928, q2 = 0.692, number of components = 3; CoMSIA r2 = 0.899, q2 = 0.701, number of components = 3) were achieved. The results obtained were graphically interpreted in terms of field contribution maps. Hence, physicochem. determinants of binding, such as steric and electrostatic and, for the first time, hydrophobic, hydrogen bond donor, and hydrogen bond acceptor properties, were mapped back onto the mol. structures of a set of nAChR modulators. In particular, changes in the binding affinity of the modulators as a result of modifications in the aromatic ring systems could be rationalized by the steric, electrostatic, hydrophobic, and hydrogen bond acceptor properties. These results were used to guide the rational design of new nAChR ligands which were subsequently synthesized for the first time and tested. Key steps of the authors synthetic approaches were successfully applied Stille and Suzuki cross-coupling reactions. Predictive r2 values of 0.614 and 0.660 for CoMFA and CoMSIA, resp., obtained for 22 in part previously unknown ligands for the (α4)2(β2)3 subtype, demonstrate the high quality of the 3D QSAR models.

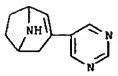
IT 540708-46-1 540708-50-7 540708-54-1
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(3D QSAR analyses-guided rational design of novel ligands for (α4)2(β2)3 nicotinic acetylcholine receptor)

RN 540708-46-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-pyrazinyl- (9CI) (CA INDEX NAME)

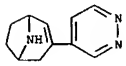


L4 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 540708-50-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(5-pyrimidinyl)- (CA INDEX NAME)

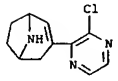


RN 540708-54-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-pyridazinyl)- (CA INDEX NAME)



IT 540708-59-6P 540709-56-6P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(3D QSAR analyses-guided rational design of novel ligands for (α4)2(β2)3 nicotinic acetylcholine receptor)

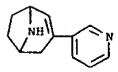
RN 540708-59-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-chloropyrazinyl)- (9CI) (CA INDEX NAME)



RN 540709-56-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-pyridinyl)-, (2Z)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 216853-22-4
CMF C12 H14 N2



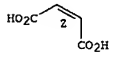
CM 2

CRN 110-16-7

L4 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

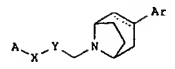
ACCESSION NUMBER: 2002:927428 CAPLUS
DOCUMENT NUMBER: 138:14010
TITLE: Preparation of aryl-8-azabicyclo[3.2.1]octanes for the treatment of depression
INVENTOR(S): Gilbert, Adam Matthew
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096906	A1	20021205	WO 2002-US16008	20020520
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
TW 589312	B	20040601	TW 2002-91110010	20020514
CA 2446532	A1	20021205	CA 2002-2446532	20020520
AU 2002303821	A1	20021209	AU 2002-303821	20020520
US 2003032645	A1	20030213	US 2002-151210	20020520
US 6632824	B2	20031014		
EP 1390364	A1	20040225	EP 2002-731881	20020520
EP 1390364	B1	20040929		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002009995	A	20040406	BR 2002-9995	20020520
CN 1509287	A	20040630	CN 2002-810261	20020520
AT 277924	T	20041015	AT 2002-731881	20020520
JP 2004533459	T	20041104	JP 2003-500085	20020520
ES 2227468	T3	20050401	ES 2002-2731881	20020520
MX 2003PA10737	A	20040302	MX 2003-PA10737	20031124

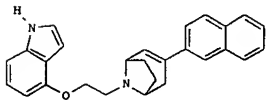
PRIORITY APPLN. INFO.: US 2001-293563P P 20010525
WO 2002-US16008 W 20020520

OTHER SOURCE(S): MARPAT 138:14010
GI

L4 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I

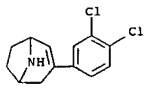


II

AB Title compds. I [X = NH, O or S; Y = (CH2)n where n = 0-3; A = (un)-substituted Ph or -pyridyl ring with addnl. possibility of being fused to an addnl. cycloalkyl or heterocyclic group using the ortho and meta positions; Ar = (un)substituted -indolyl, -Ph, -naphthyl, -anthracenyl, -phenanthrenyl, -benzyl, -benzofuryl, or -benzothienyl] are prepared and disclosed as compds. for the treatment of depression. Thus, II was prepared by N-alkylation of 3-naphththalen-2-yl-8-azabicyclo[3.2.1]oct-2-ene (preparation given) with 4-(2-chloroethoxy)-1H-indole (preparation given). I possessed IC50 values (nM) in the range of 3.5-191.0 in binding assays with cells possessing the human 5-HT transporter. The invention also includes formulations containing these compds., and methods for making and using compds. of this invention.

IT 189746-56-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antidepressant activity of arylazabicyclooctanes)

RN 189746-56-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dichlorophenyl)- (CA INDEX NAME)



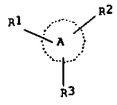
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:750728 CAPLUS
DOCUMENT NUMBER: 137:279086
TITLE: Preparation of pyrrole derivatives as antiinflammatory agents, analgesics, antiallergic agents, etc.
INVENTOR(S): Kimura, Tomio; Aoki, Kazuma; Nakao, Akira; Ushiyama, Shigeru; Shimozato, Ryuichi; Okawa, Nobuyuki
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 224 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002284779	A	20021003	JP 2002-7128	20020116

PRIORITY APPLN. INFO.: JP 2001-9601 A 20010118
OTHER SOURCE(S): MARPAT 137:279086
GI

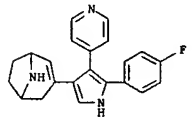


I

AB The title compds. I [ring A = pyrrole ring; R1 = (un)substituted aryl, etc.; R2 = (un)substituted heteroaryl; R3 = XR4; X = single bond, (un)substituted alkylene, etc.; R4 = (un)substituted heteroaryl, etc.; further detail related to R1, R2, and R3 is given] are prepared I inhibit cytokine production In an in vitro test using human blood treated with LPS, compds. of this invention showed IC50 values of 0.026 μM to 0.44 μM against TNF-α production Formulations are given.

IT 321344-19-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrrole derivs. as antiinflammatory agents, analgesics and antiallergic agents)

RN 321344-19-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrrol-3-yl]- (CA INDEX NAME)



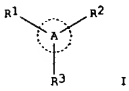
L4 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L4 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:555483 CAPLUS
DOCUMENT NUMBER: 137:125168
TITLE: Preparation of aryl(heteroaryl)pyrrole derivatives and pharmaceutical compositions containing them for prevention or treatment of hepatopathy
INVENTOR(S): Shimozato, Takaichi; Shimada, Yoko; Kimura, Tomio
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: PCT Int. Appl., 356 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057254	A1	20020725	WO 2002-JP290	20020117
W: AU, BR, CA, CN, CO, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PH, PL, RU, SG, SK, US, VN, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2435141	A1	20020725	CA 2002-2435141	20020117
AU 2002226682	A1	20020730	AU 2002-226682	20020117
JP 2002284681	A	20021003	JP 2002-8116	20020117
EP 1352906	A1	20031015	EP 2002-716313	20020117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
BR 2002006533	A	20031216	BR 2002-6533	20020117
CN 1525968	A	20040901	CN 2002-806548	20020117
MX 2003PA06468	A	20030922	MX 2003-PA6468	20030717
PRIORITY APPLN. INFO.:			JP 2001-9629 A	20010118
			WO 2002-JP290 W	20020117

OTHER SOURCE(S): MARPAT 137:125168
GI



I

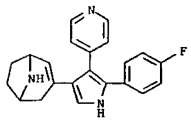
AB Disclosed are pharmaceutical compns. for the prevention or treatment of hepatopathy, containing as the active ingredient compds. represented by the general formula (I), or pharmaceutically acceptable salts, ester, or other derivs. thereof [wherein A is a pyrrole ring; R1 is optionally substituted aryl or optionally substituted heteroaryl; R2 is optionally substituted heteroaryl; and R3 is a group represented by the general formula -X-R4 [wherein X is a single bond, optionally substituted alkylene, optionally substituted alkenylene, or optionally substituted alkynylene; and R4 is substituted cycloalkyl, substituted aryl, an optionally substituted heterocyclic group, optionally substituted heteroaryl, or -NRaRb (wherein Ra and Rb are each H, alkyl, alkenyl, alkynyl, aralkyl, or alkylsulfonyl)], with the proviso that the pyrrole-constituting atoms to which R1 and R3 are bonded are each adjacent to the pyrrole-constituting atom to which R2 is bonded]. Thus, diethylphosphonoacetonitrile was treated with NaH in THF at room temperature for 1.5 h and condensed with

L4 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

2-(4-fluorophenyl)-4-formyl-3-(pyridin-4-yl)-1H-pyrrole at room temp. for 1 h to give 68% 3-[2-(4-fluorophenyl)-3-(pyridin-4-yl)-1H-pyrrol-4-yl]acrylonitrile which was hydrogenated over 10% Pd-C in a mixt. of THF and methanol at room temp. for 8 h to give 61% 4-(2-cyanoethyl)-2-(4-fluorophenyl)-3-(pyridin-4-yl)-1H-pyrrole (II). II was reduced by LiAlH4 in THF at 60° for 30 min to give 94% 4-(2-aminoethyl)-2-(4-fluorophenyl)-3-(pyridin-4-yl)-1H-pyrrole which was acylated by trifluoroacetic anhydride in THF at room temp. for 30 min to give 4-[2-(trifluoroacetylamino)ethyl]-2-(4-fluorophenyl)-3-(pyridin-4-yl)-1H-pyrrole (III). (-)-2-(4-Fluorophenyl)-4-(1,2,3,5,6,8a-hexahydroindolidin-7-yl)-3-(pyridin-4-yl)-1H-pyrrole at 10 mg/kg p.o. inhibited the increase in the level of glutamic oxaloacetic transaminase (AST) and glutamic pyruvic transaminase (ALT) by 82 and 96%, resp., in Balb/c mice suffering Con A-induced liver disorder. Pharmaceutical formulations, e.g. a dispersant contg. III, were prepd.

IT 321344-19-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aryl(heteroaryl)pyrrole derivs. for prevention or treatment of hepatopathy)

RN 321344-19-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrrol-3-yl]- (CA INDEX NAME)



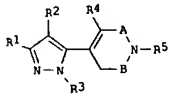
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:514291 CAPLUS
DOCUMENT NUMBER: 137:88445
TITLE: Pyrazoles and pharmaceutical compositions containing them for treatment of autoimmune diseases
INVENTOR(S): Nakatsuka, Masashi; Sasaki, Akira; Nakahira, Hiroyuki; Yokozuka, Takahiko
PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002193964	A	20020710	JP 2000-391331	20001222
PRIORITY APPLN. INFO.:			JP 2000-391331	20001222

OTHER SOURCE(S): MARPAT 137:88445
GI



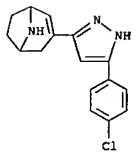
I

AB The compns., useful for treatment of ulcerative colitis, chronic rheumatoid arthritis, and multiple sclerosis, contain pyrazoles I [R1 = aralkyl, aryl; R2 = H, (un)substituted lower alkyl; R3, R5 = H, (un)substituted lower alkyl, alkenyl, protective group; R4 = H, (un)substituted lower alkyl; A = CR6R7, CHR8CH2, CH2CHR9; when A = CR6R7, then B = CR10R11; when A = CHR8CH2 or CH2CHR9, then B = single bond, CR12R13, CHR14CH2; R6-R14 = H, (un)substituted lower alkyl] or their salts. 3-(1-Ethyl-1,2,5,6-tetrahydro-3-pyridyl)-6-chloro-2,4-dihydroindeno[1,2-c]pyrazole.HCl was orally administered to mice at 50 mg/kg/day for 3 days to show 52.1% inhibition of staphylococcal enterotoxin B-induced lymph node enlargement.

IT 441005-89-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pyrazoles for treatment of autoimmune diseases)

RN 441005-89-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[5-(4-chlorophenyl)-1H-pyrazol-3-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



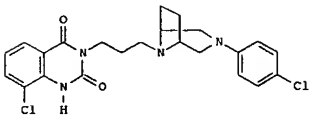
● HCl

L4 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:104660 CAPLUS
DOCUMENT NUMBER: 136:151174
TITLE: Preparation of 3-[(arylazabicycloalkyl)alkyl]quinazoline-2,4-diones as serotonin reuptake inhibitors and 5-HT2A receptor antagonists
INVENTOR(S): Butler, Todd William; Fliri, Anton Franz Josef; Gallaschun, Randall James
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 68 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1178048	A1	20020206	EP 2001-306629	20010802
EP 1178048	B1	20050615		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2354606	A1	20020203	CA 2001-2354606	20010801
CA 2354606	C	20051206		
US 2002052355	A1	20020502	US 2001-920500	20010801
US 6552015	B2	20030422		
MX 2001PA07940	A	20030820	MX 2001-PA7940	20010802
AT 297929	T	20050715	AT 2001-306629	20010802
ES 2241752	T3	20051101	ES 2001-1306629	20010802
BR 2001003210	A	20020326	BR 2001-3210	20010803
JP 2002114789	A	20020416	JP 2001-236982	20010803
JP 3803268	B2	20060802		
PRIORITY APPLN. INFO.:			US 2000-222707P P	20000803

OTHER SOURCE(S): MARPAT 136:151174
GI



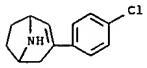
II

AB R(CH2)nZR1 [I; e.g., (un)substituted 2,4-dioxoquinazolin-3-yl; R1 = e.g., (un)substituted Ph; Z = azabicycloalkylene; n = 3 or 4] were prepared Thus, 3,2-Cl(H2N)C6H3CO2H underwent cyclocondensation/cyclization with Cl(CH2)3NCO to give 8-chloro-3,4-dihydro-2H-1-oxa-4a,9-diazaanthracene-10-one which underwent aminative ring opening with 3-(4-chlorophenyl)-3,8-diazabicyclo[3.2.1]octane to give title compound II. Data for biol. activity of I were given.

IT 189746-53-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3-[(arylazabicycloalkyl)alkyl]quinazoline-2,4-diones as

L4 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
serotonin reuptake inhibitors and 5-HT2A receptor antagonists)

RN 189746-53-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chlorophenyl)- (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

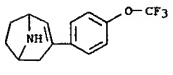
L4 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:293403 CAPLUS
DOCUMENT NUMBER: 135:354756
TITLE: Synthesis and evaluation of racemic [11C]NS2456 and its enantiomers as selective serotonin reuptake radiotracers for PET
AUTHOR(S): Smiths, D. F.; Bender, D.; Marthi, K.; Cumming, P.; Hansen, S. B.; Peters, D.; Ostergaard Nielsen, E.; Scheel-Kruger, J.; Gjedde, A.
CORPORATE SOURCE: PET Center, Aarhus University Hospitals, Aarhus, Den.
SOURCE: Nuclear Medicine and Biology (2001), 28(3), 265-270
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Positron emission tomog. (PET) radiotracers are needed for quantifying serotonin uptake sites in the living brain. Therefore, we evaluated a new selective serotonin reuptake inhibitor, NS2456, to determine whether it is suited for use in PET. Racemic NS2456 [(1RS,5SR)-8-methyl-3-[4-trifluoromethoxyphenyl]-8-azabicyclo [3.2.1]oct-2-ene] and its N-demethylated analog, racemic NS2463, selectively inhibited serotonin uptake in rat brain synaptosomes; their IC50 values were 3000-fold lower for [3H]serotonin than for either [3H]dopamine or [3H]noradrenaline. The enantiomers of NS2463 were also potent inhibitors of serotonin uptake in vitro, but they failed to show stereoselectivity. Racemic NS2463 as well as its enantiomers were radiolabeled by N-methylation with C-11, yielding [11C]NS2456 for use in PET of the living porcine brain. The compds. crossed the blood-brain barrier rapidly and accumulated preferentially in regions rich in serotonin uptake sites (e.g., brainstem, subthalamus and thalamus). However, their binding potentials were relatively low and no stereoselectivity was found. Thus, neither racemic [11C]NS2456 nor its [11C]-labeled enantiomers are ideal for PET neuroimaging of neuronal serotonin uptake sites.

IT 287110-00-3P, NS 2463
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(racemic [11C]NS2456 and its enantiomers as selective serotonin reuptake radiotracers for PET)

RN 287110-00-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(trifluoromethoxy)phenyl]- (CA INDEX NAME)

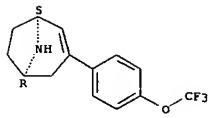


IT 372199-15-0P 372199-16-1P
RL: PUR (Purification or recovery); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(racemic [11C]NS2456 and its enantiomers as selective serotonin reuptake radiotracers for PET)

RN 372199-15-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(trifluoromethoxy)phenyl]-, (1S,5R)- (CA INDEX NAME)

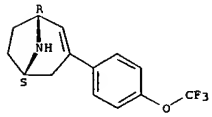
Absolute stereochemistry.

L4 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 372199-16-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(trifluoromethoxy)phenyl]-, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

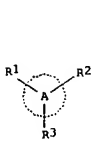
L4 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

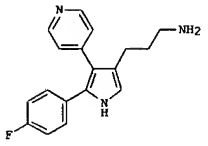
ACCESSION NUMBER: 2001:62383 CAPLUS
DOCUMENT NUMBER: 134:115858
TITLE: Preparation of heteroaryl-substituted pyrroles having excellent inhibitory activity against the production of inflammatory cytokines
INVENTOR(S): Kimura, Tomio; Aoki, Kazumasa; Nakao, Akira; Ushiyama, Shigeru; Shimozato, Takaichi; Ohkawa, Nobuyuki
PATENT ASSIGNEE(S): Sankyo Company Limited, Japan
SOURCE: Eur. Pat. Appl., 367 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1070711	A2	20010124	EP 2000-306196	20000720
EP 1070711	A3	20010131		
EP 1070711	B1	20040414		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2314373	A1	20010121	CA 2000-2314373	20000720
NO 2000003734	A	20010122	NO 2000-3734	20000720
EP 1243589	A1	20020925	EP 2002-11912	20000720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
RU 2198170	C2	20030210	RU 2000-119431	20000720
AT 264319	T	20040415	AT 2000-306196	20000720
PT 1070711	T	20040630	PT 2000-306196	20000720
ES 2216826	T3	20041101	ES 2000-306196	20000720
TW 259834	B	20060811	TW 2000-89114563	20000720
AU 200048755	A	20010201	AU 2000-48755	20000721
AU 773453	B2	20040527		
ZA 2000003705	A	20010205	ZA 2000-3705	20000721
BR 2000004534	A	20010228	BR 2000-4534	20000721
CN 1295069	A	20010516	CN 2000-131303	20000721
TR 200002120	A2	20010621	TR 2000-2120	20000721
JP 2001247564	A	20010911	JP 2000-220199	20000721
HU 2000002846	A2	20020729	HU 2000-2846	20000721
MX 2000PA07199	A	20030312	MX 2000-PA7199	20000721
HK 1033671	A1	20041119	HK 2001-104212	20010619

PRIORITY APPLN. INFO.:
JP 1999-205491 A 19990721
JP 1999-369678 A 19991227
EP 2000-306196 A3 20000720

OTHER SOURCE(S): MARPAT 134:115858
GI


I

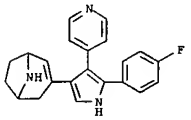

II

L4 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB The title compds. [I; A = pyrrole; R1 = (un)substituted aryl or heteroaryl; R2 = (un)substituted nitrogen-containing heteroaryl; R3 = XR4 (wherein X = a single bond, (un)substituted alkylene, alkenylene, alkynylene; R4 = substituted cycloalkyl, aryl, heterocyclyl, etc.); provided that said substituents R1 and R3 are bonded to the two atoms of said pyrrole ring which are adjacent to the atom of the pyrrole ring to which said substituent R2 is bonded] which have excellent inhibitory activity against the production of inflammatory cytokines such as TNFα (biol. data given) and IL-1β, and are useful in treating arthritis, were prepared and formulated. E.g., a multi-step synthesis of the pyrrole II was given.

IT 321344-19-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heteroaryl-substituted pyrroles having excellent inhibitory activity against the production of inflammatory cytokines)

RN 321344-19-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[5-(4-fluorophenyl)-4-(4-pyridinyl)-1H-pyrrol-3-yl]- (CA INDEX NAME)



L4 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

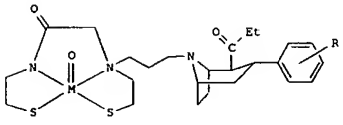
ACCESSION NUMBER: 2000:808504 CAPLUS
DOCUMENT NUMBER: 133:358543
TITLE: Preparation of rhenium and technetium complexes with tropane derivatives linked to a N2S2 chelating ligand as dopamine transporter imaging agents
INVENTOR(S): Meltzer, Peter C.; Blundell, Paul; Madras, Bertha K.; Fischman, Alan J.; Jones, Alan G.; Mahmood, Ashfaq
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA; Organix, Inc.; General Hospital Corporation
SOURCE: Eur. Pat. Appl., 56 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1051980	A2	20001115	EP 1999-121068	19991021
EP 1051980	A3	20020522		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2285516	A1	20001112	CA 2000-2285516	19991001
DE 29923477	U1	20010503	DE 1999-29923477	19991021
EP 1238978	A2	20020911	EP 2002-6707	19991021
EP 1238978	A3	20050302		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EP 1518561	A2	20050330	EP 2004-26679	19991021
EP 1518561	A3	20050406		
R: CH, DE, FR, LI				
EP 1518562	A2	20050330	EP 2004-26685	19991021
EP 1518562	A3	20050406		
R: CH, DE, FR, LI				
GB 2349882	A	20001115	GB 1999-25630	19991029
GB 2349882	B	20040811		
AU 9957162	A	20001116	AU 1999-57162	19991029
AU 783860	B2	20051215		
JP 2000319201	A	20001121	JP 1999-309599	19991029
JP 2002338569	A	20021127	JP 2002-100578	19991029
US 2002131931	A1	20020919	US 2001-975586	20011011
US 7105678	B2	20060912		
AU 2006201099	A1	20060413	AU 2006-201099	20060316
US 2007009432	A1	20070111	US 2006-517676	20060908

PRIORITY APPLN. INFO.:
US 1999-133761P P 19990512
US 1995-552584 A2 19951103
US 1997-893921 A3 19970711
US 1999-314441 A3 19990519
EP 1999-121068 A 19991021
AU 1999-57162 A3 19991029
JP 1999-309599 A3 19991029
US 2000-568106 A1 20000510
US 2000-671534 A1 20000927
US 2001-875523 A2 20010606
US 2001-975586 A1 20011011

OTHER SOURCE(S): MARPAT 133:358543
GI

L4 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

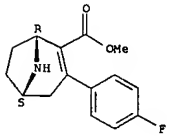

I

AB Radiopharmaceutical compds. are disclosed. A tropane compound is linked through the N atom at the 8-position to a chelating ligand capable of complexing technetium or rhenium to produce a neutral labeled complex that selectively binds to the dopamine transporter over the serotonin transporter with a ratio of ≥10. These compds. can be prepared as sep. diastereoisomers as well as a mixture of diastereoisomers. Also disclosed are radiopharmaceutical kits for preparing the labeled radiopharmaceutical compds. Thus, tropane derivative complexes (I, M = Re, 99mTc) and related complexes were prepared and DAT binding affinity was tested using Re complexes and SPECT imaging tests using 99mTc complexes were done on monkey brains treated with neurotoxin MPTP as a model study for Parkinson's disease.

IT 306740-85-2P 306740-86-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate product in preparation of rhenium and technetium complexes with tropane derivs. linked to N2S2 chelating ligand as dopamine transporter imaging agents)

RN 306740-85-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-(4-fluorophenyl)-, methyl ester, (1R,5S)- (CA INDEX NAME)

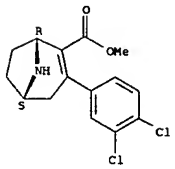
Absolute stereochemistry.



RN 306740-86-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-(3,4-dichlorophenyl)-, methyl ester, (1R,5S)- (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



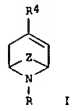
L4 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:535139 CAPLUS
DOCUMENT NUMBER: 133:150473
TITLE: Preparation of azabicycloalkenes as serotonin reuptake inhibitors
INVENTOR(S): Peters, Dan; Scheel-Kruger, Jorgen; Nielsen, Elsebet Ostergaard
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000044746	A1	20000803	WO 2000-DK38	20000128
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1149095	A1	20011031	EP 2000-901487	20000128
EP 1149095	B1	20040121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 258176	T	20040215	AT 2000-901487	20000128
US 2001047028	A1	20011129	US 2001-855630	20010515
US 6617459	B2	20030909		

PRIORITY APPLN. INFO.: DK 1999-106 A 19990128
DK 1999-950 A 19990701
WO 2000-DK38 W 20000128

OTHER SOURCE(S): MARPAT 133:150473
GI



AB Title compds. [I; R = H, (halo)alk(en)yl, alkylthio, leaving group (sic), etc.; R4 = (un)substituted Ph, -CH2Ph, -heteroaryl, a fluorescent group (sic), etc.; Z = (CH2)2-3] were prepared. Thus, 8-methyl-8-azabicyclo[3.2.1]octan-3-one was converted to the enol trifluoromethanesulfonate which was condensed with 4-BrC6H4NO2 to give I [R = Me, R4 = C6H4(NO2)-4, Z = CH2CH2]. Data for biol. activity of I were given.

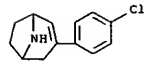
L4 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

IT 189746-54-1P 287110-00-3DP, 11C-, 18F-, or 13N-labeled 287110-00-3P 287110-01-4P 287110-02-5P 287110-07-0DP, 11C-, 18F-, or 13N-labeled 287110-07-0P 287110-08-1DP, 11C-, 18F-, or 13N-labeled 287110-08-1P 287110-09-2DP, 11C-, 18F-, or 13N-labeled 287110-09-2P 287110-11-6DP, 11C-, 18F-, or 13N-labeled 287110-11-6P 287110-12-7DP, 11C-, 18F-, or 13N-labeled 287110-12-7P 287110-14-9DP, 11C-, 18F-, or 13N-labeled 287110-14-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azabicycloalkenes as serotonin reuptake inhibitors)

RN 189746-54-1 CAPLUS
CN Propanedioic acid, compd. with 3-(4-chlorophenyl)-8-azabicyclo[3.2.1]oct-2-ene (1:1) (9CI) (CA INDEX NAME)

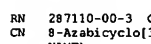
CM 1

CRN 189746-53-0
CMF C13 H14 Cl N

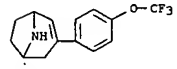


CM 2

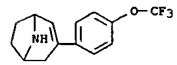
CRN 141-82-2
CMF C3 H4 O4



RN 287110-00-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(trifluoromethoxy)phenyl]- (CA INDEX NAME)



RN 287110-00-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(trifluoromethoxy)phenyl]- (CA INDEX NAME)

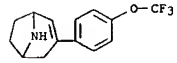


L4 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 287110-01-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(trifluoromethoxy)phenyl]-, (2E)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

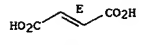
CRN 287110-00-3
CMF C14 H14 F3 N O



CM 2

CRN 110-17-8
CMF C4 H4 O4

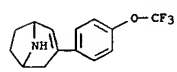
Double bond geometry as shown.



RN 287110-02-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(trifluoromethoxy)phenyl]-, (2E)-2-butenedioate (1:2) (CA INDEX NAME)

CM 1

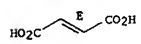
CRN 287110-00-3
CMF C14 H14 F3 N O



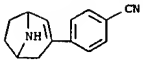
CM 2

CRN 110-17-8
CMF C4 H4 O4

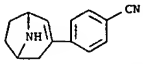
Double bond geometry as shown.



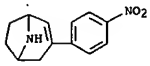
RN 287110-07-0 CAPLUS
CN Benzonitrile, 4-(8-azabicyclo[3.2.1]oct-2-en-3-yl)- (CA INDEX NAME)



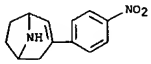
RN 287110-07-0 CAPLUS
CN Benzonitrile, 4-(8-azabicyclo[3.2.1]oct-2-en-3-yl)- (CA INDEX NAME)



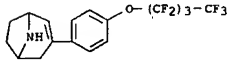
RN 287110-08-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-nitrophenyl)- (CA INDEX NAME)



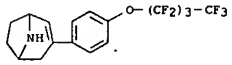
RN 287110-08-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-nitrophenyl)- (CA INDEX NAME)



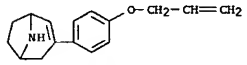
RN 287110-09-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(nonafluorobutoxy)phenyl]- (9CI) (CA INDEX NAME)



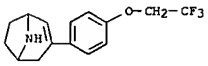
RN 287110-09-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(nonafluorobutoxy)phenyl]- (9CI) (CA INDEX NAME)



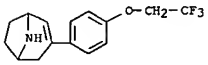
RN 287110-11-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(2,2,2-trifluoroethoxy)phenyl]- (CA



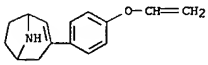
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



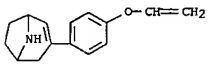
RN 287110-11-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(2,2,2-trifluoroethoxy)phenyl]- (CA INDEX NAME)



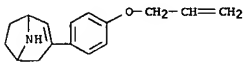
RN 287110-12-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(ethenyloxy)phenyl]- (CA INDEX NAME)



RN 287110-12-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(ethenyloxy)phenyl]- (CA INDEX NAME)



RN 287110-14-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(2-propenyloxy)phenyl]- (9CI) (CA INDEX NAME)



RN 287110-14-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(2-propenyloxy)phenyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:459206 CAPLUS
DOCUMENT NUMBER: 133:237814
TITLE: Synthesis, analgesic activity, and binding properties of some epibatidine analogs with a tropine skeleton
AUTHOR(S): Radl, Stanislav; Hafner, Wieland; Budesinsky, Milo; Hejnova, Lucie; Krejci, Ivan
CORPORATE SOURCE: Research Institute of Pharmacy and Biochemistry, Prague, 13060, Czech Rep.
SOURCE: Archiv der Pharmazie (Weinheim, Germany) (2000), 333(6), 167-174
CODEN: ARPMAS; ISSN: 0365-6233
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

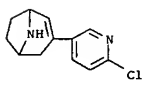
AB A series of epibatidine analogs and their positional isomers bearing an 8-azabicyclo[3.2.1]octane moiety is described. Also, some of their simplified analogs bearing a 3-piperidine moiety are reported. Their receptor binding profiles (5-HT1A, 5-HT1B, M1, M2, neuronal nicotinic receptor) and analgesic activity (hot plate, acetic acid induced writhing) have been studied. Some of the compds., especially those containing an 8-azabicyclo[3.2.1]oct-2-ene moiety, possess high affinity for the nicotinic cholinergic receptor. The most analgesically active compds. are also highly toxic. Optimized structures (PM3-MOPAC, Alchemy 2000, Tripos Inc.) were compared with that of epibatidine.

IT 259522-40-2P 259522-41-3P 292633-87-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, analgesic activity, and receptor binding properties of epibatidine analogs with tropine skeleton)

RN 259522-40-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(6-chloro-3-pyridinyl)-, (2Z)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

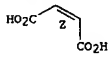
CRN 259522-30-0
CMF C12 H13 Cl N2



CM 2

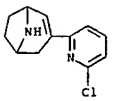
CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



L4 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 259522-41-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(6-chloro-2-pyridinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

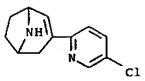


● HCl

RN 292633-87-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(5-chloro-2-pyridinyl)-, (2Z)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

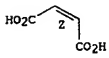
CRN 292633-83-1
CMF C12 H13 Cl N2



CM 2

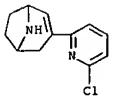
CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

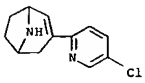


IT 259522-31-1 292633-83-1
RL: PRP (Properties)
(preparation, analgesic activity, and receptor binding properties of epibatidine analogs with tropine skeleton)
RN 259522-31-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(6-chloro-2-pyridinyl)- (CA INDEX NAME)

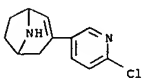
L4 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 292633-83-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(5-chloro-2-pyridinyl)- (CA INDEX NAME)



IT 259522-30-0P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, analgesic activity, and receptor binding properties of epibatidine analogs with tropine skeleton)
RN 259522-30-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(6-chloro-3-pyridinyl)- (CA INDEX NAME)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2000:384193 CAPLUS
DOCUMENT NUMBER:	133:30663
TITLE:	Preparation of 8-azabicyclo[3.2.1]oct-2-ene and -octane derivatives as cholinergic ligands at the nicotinic Acetyl Choline Receptors (nAChR)
INVENTOR(S):	Peters, Dan; Olsen, Gunnar M.; Nielsen, Simon Feldbaek; Nielsen, Elsebet Ostergaard
PATENT ASSIGNEE(S):	Neurosearch A/S, Den.
SOURCE:	PCT Int. Appl., 58 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032600	A1	20000608	WO 1999-DK661	19991126
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2342621	A1	20000608	CA 1999-2342621	19991126
EP 1133494	A1	20010919	EP 1999-973031	19991126
EP 1133494	B1	20040218		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002531456	T	20020924	JP 2000-585242	19991126
AU 761055	B2	20030529	AU 2000-13761	19991126
NZ 510287	A	20030530	NZ 1999-510287	19991126
EP 1382605	A2	20040121	EP 2003-22707	19991126
EP 1382605	A3	20040915		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 259804	T	20040315	AT 1999-973031	19991126
US 2002035122	A1	20020321	US 2001-864367	20010525
US 6680328	B2	20040120		
US 2004116703	A1	20040617	US 2003-726680	20031204
US 7045522	B2	20060516		

PRIORITY APPLN. INFO.:			
	DK 1998-1570	A	19981127
	EP 1999-973031	A3	19991126
	WO 1999-DK661	W	19991126
	US 2001-864367	A3	20010525
OTHER SOURCE(S):	MARPAT 133:30663		

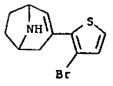
GI

I

AB The title compds. [I; R = H, alkyl, alkenyl, etc.; R1 = COR2, (un)substituted mono- or polycyclic aryl, (un)substituted (un)saturated 5-6

L4 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
membered heterocyclyl, etc.; R2 = H, alkyl, alkenyl, etc.] and their salts which are found to be cholinergic ligands at the nicotinic Acetyl Choline Receptors (no data) and may be useful for the treatment of diseases or disorders as diverse as those related to the cholinergic system of the central nervous system (CNS), diseases or disorders related to smooth muscle contraction, endocrine diseases or disorders, diseases or disorders related to neurodegeneration, diseases or disorders related to inflammation, pain, and withdrawal symptoms caused by the termination of abuse of chem. substances, were prepd. E.g., a 2-step synthesis of (±)-8-azabicyclo[3.2.1]oct-2-ene I.fumarate [R = Me; R1 = 6-methoxy-2-naphthyl] was given. Compds. I may also be useful as radioligands for in vivo receptor imaging (neuroimaging).

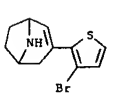
IT 273403-04-6P 273403-05-7P 273403-06-8P
273403-07-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 8-azabicyclo[3.2.1]oct-2-ene and -octane derivs. as cholinergic ligands at the nicotinic Acetyl Choline Receptors (nAChR))
RN 273403-04-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-bromo-2-thienyl)- (CA INDEX NAME)



RN 273403-05-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-bromo-2-thienyl)-, (2E)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

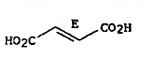
CRN 273403-04-6
CMF C11 H12 Br N S



CM 2

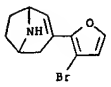
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



L4 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

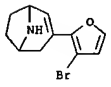
RN 273403-06-8 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-bromo-2-furanyl)- (CA INDEX NAME)



RN 273403-07-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-bromo-2-furanyl)-, (2E)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

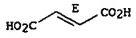
CRN 273403-06-8
CMF C11 H12 Br N O



CM 2

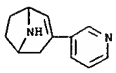
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:293414 CAPLUS
DOCUMENT NUMBER: 133:99064
TITLE: Novel potent ligands for the central nicotinic acetylcholine receptor: synthesis, receptor binding, and 3D-QSAR analysis
AUTHOR(S): Nielsen, Simon Feldbk; Nielsen, Elsebet Ostergaard; Olsen, Gunnar M.; Liljefors, Tommy; Peters, Dan
CORPORATE SOURCE: NeuroSearch A/S, Ballerup, DK-2750, Den.
SOURCE: Journal of Medicinal Chemistry (2000), 43(11), 2217-2226
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the past few years the focus on central acetylcholine receptors has shifted from compds. with affinity for muscarinic acetylcholine receptors (mAChR) to compds. with affinity for nicotinic acetylcholine receptors (nAChR). The therapeutic potential includes treatment of a variety of diseases, e.g., Alzheimer's disease, Parkinson's disease, and Tourette's syndrome. This work describes the synthesis of six novel series of potent ligands with nanomolar affinity for the α4β2 nAChR subtype. Structure-activity relationship (SAR) was evaluated by the calcn. of a 3D-QSAR model. 3D-QSAR anal. of the compds. using the GRID/GOLPE methodol. resulted in a model of high quality (R2 = 0.97, Q2 = 0.81). The coefficient plots reveal that the steric interactions between the target and our compds. are of major importance for the affinity. Bulky substituents in the 6-position of the pyridine ring will reduce the affinity of the compds., whereas bulky ring systems including a sp3-nitrogen will increase the affinity of the compds.
IT 216853-22-4P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(synthesis, receptor binding, and 3D-QSAR anal. of novel potent ligands for the central nAChR)
RN 216853-22-4 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-pyridinyl)- (CA INDEX NAME)

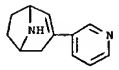


IT 216853-23-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis, receptor binding, and 3D-QSAR anal. of novel potent ligands for the central nAChR)
RN 216853-23-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-pyridinyl)-, (2E)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 216853-22-4
CMF C12 H14 N2

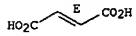
L4 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

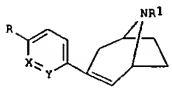
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

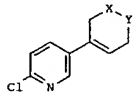


REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:30829 CAPLUS
DOCUMENT NUMBER: 132:180756
TITLE: Synthesis and binding studies of some epibatidine analogues
AUTHOR(S): Radl, Stanislav; Hezky, Petr; Hafner, Wieland; Budesinsky, Milos; Hejnova, Lucie
CORPORATE SOURCE: Research Institute of Pharmacy and Biochemistry, Prague, 130 60, Czech Rep.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(1), 55-58
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:180756
GI

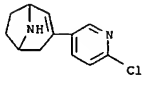


I

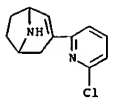


II

AB Synthesis of a series of epibatidine analogs, such as I (R = Cl, R1 = H or Me, X = N, Y = CH; R = H, R1 = H or Me, X = CCl, Y = N) and II (X = CH2, Y = NMe or NH; X = NMe, Y = CH2), bearing an 8-azabicyclo[3.2.1]octane moiety, was described. Some of the compds., especially those containing 8-azabicyclo[3.2.1]oct-2-ene moiety, show high affinity for the nicotinic cholinergic receptor.
IT 259522-30-0P 259522-31-1P 259522-40-2P
259522-41-3P 259522-42-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and nicotinic cholinergic receptor binding studies of some epibatidine analogs)
RN 259522-30-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(6-chloro-3-pyridinyl)- (CA INDEX NAME)



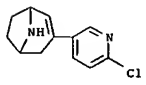
RN 259522-31-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(6-chloro-2-pyridinyl)- (CA INDEX NAME)



RN 259522-40-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(6-chloro-3-pyridinyl)-, (2Z)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

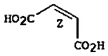
CRN 259522-30-0
CMF C12 H13 Cl N2



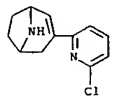
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



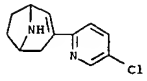
RN 259522-41-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(6-chloro-2-pyridinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 259522-42-4 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(5-chloro-2-pyridinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

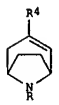
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1999:495294 CAPLUS
DOCUMENT NUMBER: 131:129909
TITLE: Preparation of 8-azabicyclo[3.2.1]oct-2-ene derivatives as radioligands for in vivo receptor imaging (neuroimaging)
INVENTOR(S): Moldt, Peter; Scheel-Kruger, Jorgen; Nielsen, Elsebet Ostergaard
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9938866	A1	19990805	WO 1999-DK44	19990128
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926099	A	19990816	AU 1999-26099	19990128
ZA 9900681	A	19990927	ZA 1999-681	19990128
EP 1068204	A1	20010117	EP 1999-906069	19990128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002501921	T	20020122	JP 2000-529334	19990128

PRIORITY APPLN. INFO.: DK 1998-125 A 19980128
WO 1999-DK44 W 19990128

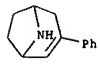
OTHER SOURCE(S): MARPAT 131:129909
GI



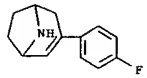
I

AB 8-Azabicyclo[3.2.1]oct-2-ene derivs. I [R = H, alkyl, haloalkyl, alkynyl, etc.; R4 = = (un)substituted Ph, CH2Ph, heteroaryl, naphthyl, fluorescent group] in labeled and unlabeled forms were prepared Labeled I were used for in vivo receptor imaging (neuroimaging) of serotonin sites. E.g., N-[11C]-Me labeled 8-methyl-3-(4-trifluoromethylphenyl)-8-azabicyclo[3.2.1]oct-2-ene (II) was prepared II was used as a marker for serotonin transporter sites (PET).
IT 36769-07-0P 163630-91-9P 189746-53-0P
189746-56-3P 234448-42-1P 234448-43-2P
234448-44-3P 234448-45-4P 234448-46-5P
234448-47-6P

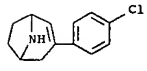
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of azabicyclooctenes as radioligands for in vivo receptor imaging (neuroimaging))
RN 36769-07-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-phenyl- (CA INDEX NAME)



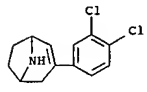
RN 163630-91-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-fluorophenyl)- (CA INDEX NAME)



RN 189746-53-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-chlorophenyl)- (CA INDEX NAME)



RN 189746-56-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dichlorophenyl)- (CA INDEX NAME)

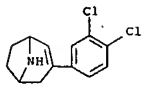


RN 234448-42-1 CAPLUS
CN Propanedioic acid, compd. with 3-(3,4-dichlorophenyl)-8-azabicyclo[3.2.1]oct-2-ene (9CI) (CA INDEX NAME)

CM 1

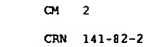
CRN 189746-56-3
CMF C13 H13 Cl2 N

L4 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

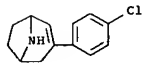
CRN 141-82-2
CMF C3 H4 O4



RN 234448-43-2 CAPLUS
CN Propanedioic acid, compd. with 3-(4-chlorophenyl)-8-azabicyclo[3.2.1]oct-2-ene (9CI) (CA INDEX NAME)

CM 1

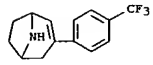
CRN 189746-53-0
CMF C13 H14 Cl N



CM 2

CRN 141-82-2
CMF C3 H4 O4

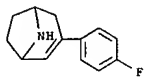
RN 234448-44-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(trifluoromethyl)phenyl]- (CA INDEX NAME)



RN 234448-45-4 CAPLUS
CN Propanedioic acid, compd. with 3-(4-fluorophenyl)-8-azabicyclo[3.2.1]oct-2-ene (9CI) (CA INDEX NAME)

L4 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CM 1

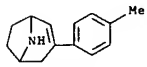
CRN 163630-91-9
CMF C13 H14 F N



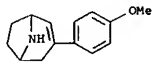
CM 2

CRN 141-82-2
CMF C3 H4 O4

RN 234448-46-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-methylphenyl)- (CA INDEX NAME)

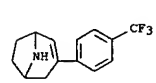


RN 234448-47-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-methoxyphenyl)- (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:451817 CAPLUS
DOCUMENT NUMBER: 131:252035
TITLE: Uptake and distribution of a new SSRI, NS2381, studied by PET in living porcine brain
AUTHOR(S): Smith, D. F.; Gee, A. D.; Hansen, S. B.; Moldt, P.; Ostergaard Nielsen, E.; Scheel-Kruger, J.; Gjedde, A.
CORPORATE SOURCE: PET Center, Aarhus University Hospitals, Aarhus, Den.
SOURCE: European Neuropsychopharmacology (1999), 9(4), 351-359
CODEN: EURNE8: ISSN: 0924-977X
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study tests the utility of a new selective serotonin reuptake inhibitor (SSRI), [11C]NS2381 ((±)-(8-[11C]methyl-3-(4-trifluoromethylphenyl)-8-azabicyclo[3.2.1]oct-2-ene)), as positron-emitting radioligand for labeling serotonin (5-HT) reuptake sites in living brain. Studies of monoamine uptake were carried out initially in vitro using rat brain synaptosomes. They showed that NS2381 and its precursor NS2435 are selective inhibitors of serotonin (5-HT) uptake. Then, studies were carried out in vivo on the uptake and distribution of [11C]NS2381 in living porcine brain. They showed that the radiotracer accumulates readily in brain, and binds reversibly in regions rich in serotonin uptake sites (e.g. raphe, basal ganglia and thalamus). In addition, [11C]NS2381 was displaced from brain tissue by the potent SSRI citalopram. The enantiomers of [11C]NS2381 were, in general, found to be similar to the racemate in terms of their uptake and distribution in living pig brain. Thus, [11C]NS2381 fulfilled several criteria of a PET radioligand for studying 5-HT uptake sites in the living brain.
IT 234448-44-3
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(uptake of the serotonin reuptake inhibitor NS2381 in brain)
RN 234448-44-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[4-(trifluoromethyl)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:795013 CAPLUS
DOCUMENT NUMBER: 130:52335
TITLE: 8-Azabicyclo[3.2.1]oct-2-ene and -octane derivatives as cholinergic ligands at nicotinic ACh receptors
INVENTOR(S): Peters, Dan; Olsen, Gunnar M.; Nielsen, Simon Feldbaek; Nielsen, Elsebet Ostergaard
PATENT ASSIGNEE(S): Neurosearch A/s, Den.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

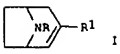
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854181	A1	19981203	WO 1998-DK225	19980529
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2289574	A1	19981203	CA 1998-2289574	19980529
CA 2289574	C	20070424		
ZA 9804639	A	19981211	ZA 1998-4639	19980529
AU 9874261	A	19981230	AU 1998-74261	19980529
AU 745964	B2	20020411		
EP 984965	A1	20000315	EP 1998-921378	19980529
EP 984965	B1	20040519		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 9902942	T2	20000421	TR 1999-2942	19980529
EE 9900529	A	20000615	EE 1999-529	19980529
EE 4057	B1	20030616		
BR 9809697	A	20000711	BR 1998-9697	19980529
HU 2000002713	A2	20010129	HU 2000-2713	19980529
HU 2000002713	A3	20010228		
NZ 500642	A	20011130	NZ 1998-500642	19980529
JP 2002501514	T	20020115	JP 1999-500130	19980529
RU 2186780	C2	20020810	RU 1999-128075	19980529
AT 267199	T	20040615	AT 1998-921378	19980529
PL 190567	B1	20051230	PL 1998-337054	19980529
SK 284994	B6	20060406	SK 1999-1626	19980529
NO 9905850	A	19991129	NO 1999-5850	19991129
US 6645977	B1	20031111	US 1999-450637	19991129
MX 9911081	A	20000831	MX 1999-11081	19991130
HK 1027353	A1	20050107	HK 2000-106419	20001010
US 2004019207	A1	20040129	US 2003-620559	20030717
US 6964972	B2	20051115		

PRIORITY APPLN. INFO.:

DK 1997-627	A	19970530
DK 1997-1502	A	19971219
DK 1998-408	A	19980324
DK 1998-534	A	19980416
WO 1998-DK225	W	19980529
US 1999-450637	A3	19991129

OTHER SOURCE(S): MARPAT 130:52335
GI

L4 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I

AB Title compds. I (R = H, alkyl, alkenyl, aryl, aralkyl, etc.; R1 = acyl, aryl, heteroaryl, etc.) or their saturated analogs were prepared by several methods. Thus, endo-8-benzyl-3-hydroxy-3-(3-pyridyl)-8-azabicyclo[3.2.1]octane (II) was prepared in 34% yield from 8-benzyl-8-azabicyclo[3.2.1]octan-3-one and 3-bromopyridine, and II was then converted to I (R = benzyl, R1 = 3-pyridyl) in 78% yield. The latter was converted to the fumarate salt. The affinity of the products for nicotinic ACh receptors was examined in tests of 3H-cytisine, 3H-epibatidin, and 3H-α-bungarotoxin binding.

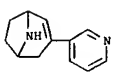
IT 216853-23-5P 216853-56-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(8-azabicyclo[3.2.1]oct-2-ene and -octane derivs. as cholinergic ligands at nicotinic ACh receptors)

RN 216853-23-5 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3-pyridinyl)-, (2E)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

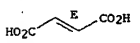
CRN 216853-22-4
CMF C12 H14 N2



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



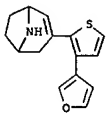
RN 216853-56-4 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[3-(3-furanyl)-2-thienyl]-, (2E)-2-butenedioate (1:1) (CA INDEX NAME)

CM 1

CRN 216853-55-3
CMF C15 H15 N O S

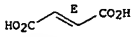
L4 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:372147 CAPLUS
DOCUMENT NUMBER: 126:343505
TITLE: Preparation of 8-azabicyclo[3.2.1]oct-2-enes as serotonin reuptake inhibitors
INVENTOR(S): Moldt, Peter; Scheel-Krueger, Joergen; Olsen, Gunnar M.; Nielsen, Elsebet Oestergaard
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9713770	A1	19970417	WO 1996-EP4449	19961011
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI				
CA 2233541	A1	19970417	CA 1996-2233541	19961011
CA 2233541	C	20020430		
AU 9672917	A	19970430	AU 1996-72917	19961011
AU 709327	B2	19990826		
EP 859777	A1	19980826	EP 1996-934662	19961011
EP 859777	B1	20070523		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1199400	A	19981118	CN 1996-197566	19961011
CN 1083840	B	20020501		
JP 10512589	T	19981202	JP 1997-514726	19961011
JP 3462505	B2	20031105		
BR 9610960	A	19990302	BR 1996-10960	19961011
HU 9802433	A2	19990428	HU 1998-2433	19961011
CZ 285093	B6	19990512	CZ 1998-758	19961011
RU 2157372	C2	20001010	RU 1998-105169	19961011
EE 3446	B1	20010615	EE 1998-62	19961011
PL 185357	B1	20030430	PL 1996-326195	19961011
SK 283425	B6	20030701	SK 1998-287	19961011
IL 123583	A	20030731	IL 1996-123583	19961011
AT 362931	T	20070615	AT 1996-934662	19961011
NO 9800919	A	19980608	NO 1998-919	19980303
US 6100275	A	20000808	US 1998-43294	19980518
PRIORITY APPLN. INFO.:			DK 1995-1156 A	19951013
			WO 1996-EP4449 W	19961011

OTHER SOURCE(S): MARPAT 126:343505
GI

I

L4 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB Title compds. [I; R = H, (cyclo)alkyl, CH2CH2OH, etc.; R1 = (un)substituted Ph, -naphthyl, -heteroaryl, etc.] were prepared Thus, 8-methyl-8-azabicyclo[3.2.1]octan-3-one was condensed with 3,4-Cl2C6H3Br and the product dehydrated to give I (R = Me, R1 = C6H3Cl2-3,4). Data for biol. activity of I prepared I were given.

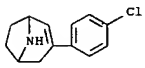
IT 189746-54-1P 189746-56-3P 189746-57-4P
189880-62-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 8-azabicyclo[3.2.1]oct-2-enes as serotonin reuptake inhibitors)

RN 189746-54-1 CAPLUS

CN Propanedioic acid, compd. with 3-(4-chlorophenyl)-8-azabicyclo[3.2.1]oct-2-ene (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 189746-53-0
CMF C13 H14 Cl N

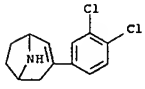


CM 2

CRN 141-82-2
CMF C3 H4 O4

RN 189746-56-3 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(3,4-dichlorophenyl)- (CA INDEX NAME)



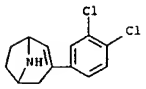
RN 189746-57-4 CAPLUS

CN Propanedioic acid, compd. with 3-(3,4-dichlorophenyl)-8-azabicyclo[3.2.1]oct-2-ene (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 189746-56-3
CMF C13 H13 Cl2 N

L4 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

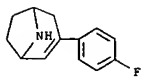
CRN 141-82-2
CMF C3 H4 O4

$HO_2C-CH_2-CO_2H$

RN 189880-62-4 CAPLUS
CN Propanedioic acid, compd. with 3-(4-fluorophenyl)-8-azabicyclo[3.2.1]oct-2-ene (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 163630-91-9
CMF C13 H14 F N



CM 2

CRN 141-82-2
CMF C3 H4 O4

$HO_2C-CH_2-CO_2H$

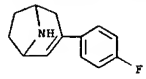
L4 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:568952 CAPLUS
DOCUMENT NUMBER: 123:282
TITLE: σ Ligands with Subnanomolar Affinity and Preference for the σ2 Binding Site. 1. 3-(ω-Aminoalkyl)-1H-indoles
AUTHOR(S): Perregaard, Jens; Moltzen, Ejner K.; Meier, Eddi; Sanchez, Connie
CORPORATE SOURCE: Research and Development, H. Lundbeck A/S, Copenhagen-Valby, DK-2500, Den.
SOURCE: Journal of Medicinal Chemistry (1995), 38(11), 1998-2008
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 123:282
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A series of 4-(1H-indol-3-yl)-1-butyl-substituted 4-phenylpiperidines, 4-phenyl-1,2,3,6-tetrahydropyridines, and 4-phenylpiperazines was synthesized. The Ph group was optionally substituted with 4-fluoro or 2-methoxy substituents. High affinity for both σ1 and σ2 binding sites was achieved with these compds. Addnl., these compds. had relatively high affinity for serotonin 5-HT1A and 5-HT2A, dopamine D2, and adrenergic α1 receptors. Introduction of a 4-fluorophenyl substituent at the indole nitrogen atom rendered very selective σ2 ligands with subnanomolar affinity for the σ2 binding site. The prototype of such a compound was I. This compound had the following binding affinities: IC50 (σ1) = 16 nM, IC50 (σ2) = 0.27 nM, IC50 (5-HT1A) = 22 000 nM, IC50 (5-HT2A) = 270 nM, IC50 (D2) = 4200 nM, IC50 (α1) = 220 nM. Spiro-joining of the Ph and the piperidine rings into a spiro[isobenzofuran-1(3H),4'-piperidine] ring system resulted in even more selective compds. Variations of the 1-substituent at the indole and of the chain length of the alkylene spacer group were studied. The optimal compound was the spiro analog of I. This compound (II) had the binding affinities: IC50 (σ1) = 17 nM, IC50 (σ2) = 0.12 nM, IC50 (5-HT1A) = 21 000 nM, IC50 (5-HT2A) = 2000 nM, IC50 (D2) = 800 nM, IC50 (α1) = 330 nM. However, the most selective σ2 vs. σ1 ligand was the tropane derivative (III). This compound had the following binding affinities: IC50 (σ1) = 1200 nM, IC50 (σ2) = 2.5 nM. Potent anxiolytic activity in the black/white box exploration test in rats was found with the two most prominent σ2 ligands Lu 29-253 and Lu 28-179. Good penetration into the CNS was documented both after s.c. and peroral administration of Lu 28-179 by ex vivo binding studies. Long duration of action was demonstrated both in ex vivo binding (T1/2 .apprx. 20 h) and in the black/white box exploration test.
IT 163630-91-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(σ ligands with subnanomolar affinity and preference for the σ2 binding site: aminoalkylindoles)
RN 163630-91-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-(4-fluorophenyl)- (CA INDEX NAME)

L4 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

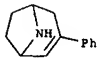


L4 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1972:405360 CAPLUS
DOCUMENT NUMBER: 77:5360
ORIGINAL REFERENCE NO.: 77:939a,942a
TITLE: Antispasmodic 8-carbamoyl-3-phenylnortropanes
INVENTOR(S): Helsley, Grover C.
PATENT ASSIGNEE(S): A. H. Robins Co., Inc.
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

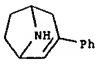
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2143587	A	19720309	DE 1971-2143587	19710831
US 3657257	A	19720418	US 1970-68592	19700831
GB 1304649	A	19730124	GB 1971-37953	19710812
AU 7132717	A	19730301	AU 1971-32717	19710825
ES 394509	A1	19741116	ES 1971-394509	19710825
JP 51016438	B	19760524	JP 1971-64817	19710826
FR 2103642	A1	19720414	FR 1971-31358	19710830
FR 2103642	A5	19720414		
ZA 7105770	A	19720426	ZA 1971-5770	19710830
CA 941379	A1	19740205	CA 1971-121714	19710830
CH 552588	A	19740815	CH 1971-12693	19710830

PRIORITY APPLN. INFO.: US 1970-68592 A 19700831
GI For diagram(s), see printed CA Issue.
AB Four title compds. (I, R = H2NCO or EtNHCO, R1 = H or CF3) were prepared by reaction of I (R = H) with H2NCONHNO2 or EtNCO. Addnl., 8-carbamoyl-3β-phenylnortropane (II) was prepared in 17% yield by refluxing 8-cyano-3β-phenylnortropane with 6N HCl 16 hr. I and II had antispasmodic effects in mice, ED50 = 45-100 mg/kg. Thus, refluxing 3-phenylnortropanol, prepared in 78% yield by hydrogenation of its 8-benzyl derivative in EtOH over Pd/C, with 6 N HCl for 16 hr gave 79% 3-phenylnortropidine-HCl (III). Hydrogenation of III over Pd/C in EtOH yielded I (R = R1 = H), which on refluxing with H2NCONHNO2 in EtOH for 1 hr gave 59% I (R = H2NCO, R1 = H).
IT 36769-06-9P 36769-07-0P 36769-08-1P
36769-09-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 36769-06-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-phenyl-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

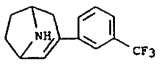
RN 36769-07-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-phenyl- (CA INDEX NAME)



RN 36769-08-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[3-(trifluoromethyl)phenyl]-, ethanedioate (1:1) (CA INDEX NAME)

CM 1

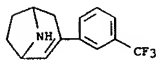
CRN 36769-09-2
CMF C14 H14 F3 N



CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 36769-09-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene, 3-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



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FULL ESTIMATED COST	198.75	371.06

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NEWS 3	AUG 06	FSTA enhanced with new thesaurus edition
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NEWS 5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 7	AUG 27	USPATOLD now available on STN
NEWS 8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 10	SEP 13	FORIS renamed to SOFIS
NEWS 11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 16	OCT 19	BEILSTEIN updated with new compounds
NEWS 17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 18	NOV 19	WPIX enhanced with XML display format
NEWS 19	NOV 30	ICSD reloaded with enhancements
NEWS 20	DEC 04	LINPADOCDB now available on STN
NEWS 21	DEC 14	BEILSTEIN pricing structure to change
NEWS 22	DEC 17	USPATOLD added to additional database clusters
NEWS 23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 24	DEC 17	DGENE now includes more than 10 million sequences
NEWS 25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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FILE LAST UPDATED: 25 Dec 2007 (20071225/ED)

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http://www.cas.org/infopolicy.html

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           173 RENINS
         30059 RENIN
                 (RENIN OR RENINS)
         65897 ANGIOTENSIN
          1757 ANGIOTENSINS
         65989 ANGIOTENSIN
                 (ANGIOTENSIN OR ANGIOTENSINS)
       3664344 SYSTEM?
L1       11116 RENIN ANGIOTENSIN SYSTEM?
                 (RENIN(W)ANGIOTENSIN(W)SYSTEM?)

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        275922 DISEASES
       1140646 DISEASE
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         35306 RAS
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        35307 RAS
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            0 ASSPCIAT?
L4          0 L3 AND ASSPCIAT?

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            1 ASSOCDS
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       266282 ASSOCN
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                (ASSOCN OR ASSOCNS)
      1461648 ASSOCIAT?
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L6        126 L5 AND PY<2003

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L7         56 L6 AND HYPERTENSION?

=> s l7 and cardiac?
       136950 CARDIAC?
L8         17 L7 AND CARDIAC?

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L8 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:929536 CAPLUS
DOCUMENT NUMBER: 138:167583
TITLE: The renin-angiotensin system as a risk factor and therapeutic target for cardiovascular and renal disease
AUTHOR(S): Volpe, Massimo; Savoia, Carmine; De Paolis, Paola; Ostrowska, Beata; Tarasi, David; Rubattu, Speranza
CORPORATE SOURCE: Department of Experimental Medicine and Pathology, University of Rome "La Sapienza", Italy
SOURCE: Journal of the American Society of Nephrology (2002), 13(Suppl. 3), S173-S178
CODEN: JASNEU; ISSN: 1046-6673
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The renin-angiotensin system (RAS) plays an important homeostatic role in BP regulation, water and salt balance, and tissue growth control under physiol. conditions. On the other hand, a pivotal involvement of the RAS in the pathophysiol. of cardiovascular and renal disease is extensively supported by both basic and clin. evidence. In particular, it is today recognized that angiotensin II (AngII), the biol. effector of the RAS, may prompt a number of relevant structural and functional abnormalities through the activation of a complex of cellular effects mostly mediated via its binding with the AT1 subtype receptors. The key role of these AngII-linked mechanisms of disease is strongly corroborated by large interventional studies. In fact, pharmacol. interference with RAS activity, by both preventing AngII formation with angiotensin-converting enzyme inhibitors or antagonizing its binding to cell membrane receptors by selective antagonists, is associated with highly beneficial outcomes in major disease conditions (hypertension, diabetes, renal failure, heart failure, myocardial infarction, stroke, and others). This article briefly reviews the current views on the biol. organization of RAS evidence supporting a pathogenic role of the RAS activity in promoting cardiac, vascular, and renal disease, and finally provides the basis for considering inhibition of RAS activity a major target for therapeutic interventions in these conditions.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:891527 CAPLUS
DOCUMENT NUMBER: 138:167864
TITLE: AGT and AT1R gene polymorphism in hypertensive heart disease
AUTHOR(S): Mettimano, M.; Romano-Spica, V.; Iannf, A.; Specchia, M. L.; Migneco, A.; Savi, L.
CORPORATE SOURCE: Hypertension Centre, Department of Internal Medicine, Catholic University Medical School, Rome, Italy
SOURCE: International Journal of Clinical Practice (2002), 56(8), 574-577
CODEN: IJCPF9; ISSN: 1368-5031
PUBLISHER: Medicom International
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Left ventricular hypertrophy in patients with hypertension is a main clin. prognostic entity. The aim of this study was to evaluate the association between mutations at genes of the renin-angiotensin system (RAS) and the development of left ventricular hypertrophy Genetic polymorphism in angiotensinogen (AGT) and angiotensin II-type 1 receptor (AT1R) genes was examined in a group of well-selected essential hypertensive Caucasians with left ventricular involvement (n=40) and a group of healthy unrelated caucasians (n=150). Cardiac morphol. and function were assessed by M-mode echocardiog. Mol. variants were analyzed by amplified fragment length polymorphism. We observed a statistically significant difference both for AGT and AT1R genotype distribution in patients with left ventricular hypertrophy compared with controls ($p<0.05$). A 0.49 and 0.225 frequency was detected among cases for T and C mutant alleles at AGT and AT1R genes. Mutations in RAS genes are involved in the pathophysiol. of target-organ damage in essential hypertension. Evaluation of mol. factors conferring a risk of developing heart involvement may lead to better identification of patient subgroups and more effective control of the clin. course.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:133158 CAPLUS
DOCUMENT NUMBER: 137:76980
TITLE: The renin-angiotensin and adrenergic nervous system in cardiac hypertrophy in fructose-fed rats
AUTHOR(S): Kamide, Kei; Rakugi, Hiromi; Higaki, Jitsuo; Okamura, Atsunori; Nagai, Michiko; Moriguchi, Kouichi; Ohishi, Mitsuru; Satoh, Noriyuki; Tuck, Michael L.; Ogihara, Toshio
CORPORATE SOURCE: Department of Geriatric Medicine, Osaka University Medical School, Suita, 565-0871, Japan
SOURCE: American Journal of Hypertension (2002), 15(1, Pt. 1), 66-71
CODEN: AJHYE6; ISSN: 0895-7061
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Hyperinsulinemia and insulin resistance are associated with left ventricular hypertrophy (LVH) and cardiovascular complications in hypertensive subjects. The aim of this study was to explore the mechanisms for LVH including activation of the renin-angiotensin system system (RAS) and the sympathetic nervous system and their activation by insulin using a rat model of hyperinsulinemia and insulin resistance. Methods: Male Sprague-Dawley rats were fed a high-fructose or control diet. The fructose-fed rats (FFR) were divided into four subgroups that were administrated either vehicle or the following antihypertensive drugs (n = 6-8) for 4 wk: 1) olmesartan, an angiotensin II type 1 (AT1) receptor antagonist; 2) bunazosin, an α1-receptor blocker; and 3) hydralazine, a direct vasodilator. Results: Fructose feeding induced significant increases in mean systolic blood pressure (BP) levels at 4 wk (control, 117 v fructose, 131 mm Hg), left ventricular weight, and the sum of the insulin level in response to a glucose tolerance test (2 g/kg). Fructose feeding also increased urinary excretion of epinephrine and norepinephrine, the d. of cardiac α1-adrenergic receptors, and the content of angiotensin II in the left ventricle. All antihypertensive drugs decreased systolic BP, but only the AT1 receptor antagonist attenuated the development of LVH in FFR. The AT1 receptor antagonist did not affect glucose-mediated insulin responses, but did suppress urinary catecholamine excretion and cardiac α1-adrenergic receptor d. Conclusions: Left ventricular hypertrophy in FFR may be less dependent on systemic elevations of BP and more dependent on the RAS and the sympathetic nervous system. Use of an AT1 receptor antagonist might be the most beneficial way to prevent progression of LVH through direct effects on tissue RAS and the sympathetic nervous system in FFR. As these changes occur in a rat model with hyperinsulinemia, insulin may have a role in promoting LVH by activating the local RAS and sympathetic nervous system activity.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:8864 CAPLUS
DOCUMENT NUMBER: 136:198036
TITLE: Molecular interactions of vasoactive systems in cardiovascular damage
AUTHOR(S): Bader, Michael
CORPORATE SOURCE: Max-Delbruck-Center for Molecular Medicine (MDC), Berlin, D-13092, Germany
SOURCE: Journal of Cardiovascular Pharmacology (2001), 38(Suppl. 2), S7-S9
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The renin-angiotensin system (RAS) and the kallikrein-kinin system (KKS) are important in the etiol. of hypertension and the pathogenesis of cardiac and renal damage associated with elevated blood pressure. While angiotensin II acts by increasing blood pressure and supporting end-organ damage, kinins have an opposite protective effect. The two systems interact on many levels. Angiotensin-converting enzyme (ACE) activates angiotensins and inactivates kinins. ACE inhibitors therefore exert their organ-protective action via both systems, as they block the deleterious RAS and potentiate the protective KKS. Furthermore, ACE may directly interact with the kinin B2 receptor and ACE inhibitors, thereby eliciting a resensitization of this receptor following agonist-induced desensitization. Recently, a functional heterodimer of AT1 and B2 receptors has also been demonstrated. Moreover, kallikreins may be involved in the activation of prorenin and in the signaling pathway of angiotensin AT2 receptors. Because of the multitude of interactions, any therapeutic intervention into one of the two peptide systems will automatically lead to an alteration in the other. This double action is utilized by drugs such as ACE inhibitors to provide unprecedented effectiveness in hypertension and associated cardiac and renal damage.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:311138 CAPLUS
DOCUMENT NUMBER: 135:251665
TITLE: Regression of cardiac hypertrophy in the SHR by combined renin-angiotensin system blockade and dietary sodium restriction
AUTHOR(S): Abro, Emad; Griffiths, Cory D.; Morgan, Trefor O.; Delbridge, Lea M. D.
CORPORATE SOURCE: Department of Physiology, University of Melbourne, Parkville, 3010, Australia
SOURCE: JRAAS (2001), 2(Suppl. 1), S148-S153
CODEN: JRAAAG; ISSN: 1470-3203
PUBLISHER: JRAAS Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study investigated the cardiac effects of renin-angiotensin system (RAS) blockade in the spontaneously hypertensive rat (SHR) by using cotreatment with an angiotensin II receptor blocker (ARB) and an angiotensin-converting enzyme (ACE) inhibitor in combination with different sodium intakes. In SHR, at high levels of sodium intake (4.0%), aggressive RAS blockade with the ARB candesartan cilexetil (3 mg/kg) and the ACE inhibitor perindopril (6 mg/kg) did not result in regression of cardiac hypertrophy. In contrast, RAS blockade coupled with reduced sodium diet (0.2%) regressed cardiac hypertrophy, impaired animal growth and was associated with elevated plasma renin and dramatically suppressed plasma angiotensinogen levels. Histol. analyses indicated that the differential effect of reduced sodium on heart growth during RAS blockade was not associated with any change in myocardial interstitial collagen, but reflected modification of cellular geometry. Dimensional measurements of enzymically isolated ventricular myocytes showed that, in the RAS-blocked, reduced-sodium group, myocyte length and width were decreased by about 16-19% compared with myocytes from the high-sodium group. The findings highlight the importance of "titrating" sodium intake with combined RAS blockade in the clin. setting to optimize therapeutic benefit.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:80625 CAPLUS
DOCUMENT NUMBER: 134:264452
TITLE: Renin-angiotensin system contribution to cardiac hypertrophy in experimental hyperthyroidism: an echocardiographic study
AUTHOR(S): Basset, Alexandra; Blanc, Jocelyne; Messas, Emmanuel; Hagege, Albert; Elghozi, Jean-Luc
CORPORATE SOURCE: Laboratoire de Pharmacologie, Faculte de Medecine Necker, Hopital Europeen Georges Pompidou, Paris, 75015, Fr.
SOURCE: Journal of Cardiovascular Pharmacology (2001), 37(2), 163-172
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of this study was to evaluate, using echocardiog., the involvement of the renin-angiotensin system (RAS) in left ventricular (LV) hypertrophy development in exptl. hyperthyroidism. Thyrotoxicosis was produced by a daily i.p. injection of L-thyroxine (T4), 0.1 mg/kg per day for 15 days in Wistar rats. Control (euthyroid) rats received i.p. daily injection of the thyroxine solvent. Two series of expts. were performed. In the first series, euthyroid (n = 10) and hyperthyroid (n = 14) rats were surgically prepared with a femoral artery catheter. After a 3-day recovery period, blood pressure and heart rate were measured and blood samples were collected in conscious and unrestrained rats. In the second series of experiment, measurement of LV geometry was realized with two-dimensional time-movement echocardiog. on the 15th day of treatment in control conditions and after long-term treatment with the angiotensin II type 1 receptor antagonist valsartan (10 mg/kg per day for 15 days) in both euthyroid and hyperthyroid rats. The dose and duration of T4 treatment was sufficient to induce a significant degree of hyperthyroidism with characteristic features including tachycardia, systolic hypertension, myocardial hypertrophy, hyperthermia, and weight loss. In addition, we measured an increase in free fractions of thyroid hormones, and a threefold increase in plasma renin activity. Echocardiog. examns. in rats revealed a strong correlation between LV weight and echocardiog. LV mass. Hyperthyroid rats exhibited an increased LV mass with a marked increase in the LV end-diastolic posterior wall and septal thickness. Chronic treatment with valsartan prevented this concentric LV hypertrophy ($p < 0.01$), with full prevention of the LV posterior wall hypertrophy ($p < 0.001$) and decreased LV septal hypertrophy ($p < 0.05$). In conclusion, the cardiovascular alterations of hyperthyroidism were reproduced with thyroid hormone injections in rats. Activation of the RAS in hyperthyroid rats was accompanied by increased LV mass. Using valsartan, we demonstrated that the RAS impinged on the LV remodelling in our exptl. hyperthyroidism model. A chronic treatment with an angiotensin II type I receptor antagonist prevented the development of the concentric LV hypertrophy assocd . with thyrotoxicosis.
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:873755 CAPLUS
DOCUMENT NUMBER: 134:142222
TITLE: Contribution of circulating renin to local synthesis of angiotensin peptides in the heart
AUTHOR(S): Prescott, Gary; Silversides, David W.; Chiu, Sui Mei Linda; Reudelhuber, Timothy L.
CORPORATE SOURCE: Laboratory of Molecular Biochemistry of Hypertension, Clinical Research Institute of Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: Physiological Genomics [online computer file] (2000), 4, 67-73
CODEN: PHGEFP; ISSN: 1094-8341
URL: http://physiolgenomics.physiology.org/cgi/reprint/4/1/67.pdf
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB The activity of a local cardiac renin-angiotensin system (RAS) has long been suspected in the promotion of cardiac pathologies including hypertrophy, ischemia, and infarction. All of the components of the RAS cascade have been demonstrated to be synthesized within the heart with the possible exception of the first enzyme in the cascade, renin. In the current study, the authors provide direct evidence that circulating renin can contribute to cardiac-specific synthesis of angiotensin peptides. Furthermore, the authors demonstrate this effect is independent of blood pressure and that in animals of comparable blood pressure, elevated circulating renin significantly enhances cardiac fibrosis. These results may serve to explain some of the cardiac pathologies associated with the RAS.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:743378 CAPLUS
DOCUMENT NUMBER: 134:260734
TITLE: Angiotensin II type 1 receptor blockade: A novel therapeutic concept
AUTHOR(S): Johnston, Colin I.
CORPORATE SOURCE: Department of Medicine Austin and Repatriation Medical Centre, University of Melbourne, Melbourne, Australia
SOURCE: Blood Pressure, Supplement (2000), (1), 9-13
CODEN: BPSUEY; ISSN: 0803-8023
PUBLISHER: Scandinavian University Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 31 refs. Angiotensin II type 1 (AT1 receptor blockers, such as candesartan, are attractive alternatives to ACE inhibitors in the treatment of hypertension and cardiovascular disease. Although angiotensin-converting enzyme (ACE) inhibitors are able to suppress the renin-angiotensin system (RAS), their mechanism of action may limit their clin. utility in the treatment of hypertension. For example, they act as competitive inhibitors of ACE. This means that their effects can be overcome by high levels of angiotensin I, which occur after ACE inhibition due to removal of the neg. feedback effect of angiotensin II on renal renin release. ACE inhibitors are also unable to block the production of angiotensin II by non-ACE-mediated pathways. Furthermore, ACE is not a specific enzyme. Its inhibition therefore has effects on other substances, such as bradykinin, leading to the class-specific side effects associated with ACE inhibitors. Candesartan, on the other hand, binds insurmountably to the AT1-receptor, thereby providing more complete blockade of the neg. cardiovascular effects of angiotensin II than is possible with ACE inhibitors. The specificity of AT1-receptor blockade also ensures that efficacy is achieved without inducing the side effect of cough that results from the non-specific consequences of ACE inhibition. Preclin. and early clin. studies demonstrate that AT1-receptor blockers produce at least the same degree of target-organ protection as has been demonstrated for ACE inhibitors. Addnl. benefits of AT1-receptor blockers may arise from the fact that, unlike ACE inhibitors, they do not prevent the activity of angiotensin II AT2-receptors AT2-receptors in the heart, which is thought to reduce cardiac remodelling. From a mechanistic perspective, therefore, AT1-receptor blockers appear to have advantages over ACE inhibitors, in terms of a more complete blockade of angiotensin II effects, while also avoiding the specific side effects associated with ACE inhibition.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:182216 CAPLUS
DOCUMENT NUMBER: 133:87615
TITLE: Angiotensin-converting enzyme gene I/D polymorphism and carotid artery disease in renovascular hypertension
AUTHOR(S): Losito, Attilio; Selvi, Antonio; Jeffery, Steve; Afzal, Ali R.; Parente, Basso; Cao, Pier Giorgio
CORPORATE SOURCE: Unita Operativa Nefrologia e Dialisi Policlinico, Perugia, 06100, Italy
SOURCE: American Journal of Hypertension (2000), 13(2), 128-133
CODEN: AJHYE6; ISSN: 0895-7061
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB There is evidence linking the activation of the renin-angiotensin system (RAS) with target organ damage in renovascular hypertension (RVH). A genetic association of the DD genotype of the angiotensin-converting enzyme (ACE) gene with cardiovascular complications has been found in various clin. conditions. The aim of our study was to determine whether the insertion/deletion (I/D) polymorphism of the ACE gene is associated with the high prevalence of target organ damage reported in RVH. A total of 65 atherosclerotic patients (age 68.2 ± 5.2 yr) with RVH and 49 atherosclerotic patients (age 68.0 ± 6.3 yr) with essential hypertension (EH) were sequentially enrolled when attending the outpatient clinic for specialist assessment of their vascular disorder. Cardiac, renal, and vascular involvement were assessed in both groups and blood was taken for genetic anal. Patients with RVH had a higher prevalence of left ventricular hypertrophy (LVH), carotid artery disease, and albuminuria than those with EH. In RVH, but not in EH, the DD genotype was significantly associated with severe arterial disease. In RVH, carotid disease (lumen narrowing >60%) was present in 62% of DD patients vs. 25% of the other genotypes (OR = 4.90, 95% CI: 1.70-14.13). Such an association was also present in peripheral vascular disease: 72.4% in DD patients vs. 41.6% in the other genotypes (OR = 3.67, 95% CI = 1.29-10.36). Logistic regression anal. showed that the DD genotype was the strongest predictor of risk of severe carotid disease. We conclude that, in atherosclerotic RVH, there is an association of the severity of vascular disease with the DD genotype of the ACE gene.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:740140 CAPLUS
DOCUMENT NUMBER: 132:206328
TITLE: Augmented expression of cardiac atrial natriuretic peptide system in hypertensive rats
AUTHOR(S): An, Mi Ra; Chung, Yoo Jeong; Kang, Dae Gill; Nam, Sang Chae; Lee, JongUn
CORPORATE SOURCE: Department of Physiology, Chonnam National University Medical School, Kwangju, 500-757, S. Korea
SOURCE: Journal of Korean Medical Science (1999), 14(5), 497-501
CODEN: JKMSEH; ISSN: 1011-8934
PUBLISHER: Korean Academy of Medical Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was aimed at investigating the regulation of atrial natriuretic peptide (ANP) system in association with either enhanced or attenuated activity of the renin-angiotensin system (RAS). The cardiac tissue mRNA and peptide levels of ANP were measured in rats with two-kidney, one clip (2K1C) or deoxy-corticosterone acetate (DOCA)-salt hypertension. Plasma renin concentration was increased in 2K1C hypertension along with increases of renin mRNA and protein contents in the clipped kidney. On the contrary, it was suppressed in DOCA-salt hypertension along with decreases of renin mRNA and protein contents in the remaining kidney. The plasma ANP concentration was similarly increased in both models of hypertension. The cardiac tissue ANP contents were not significantly changed, but the tissue ANP mRNA levels were upregulated in the hypertrophied heart in these two models of hypertension. It is suggested that the cardiac ANP system is transcriptionally enhanced by cardiac hypertrophy associated with hypertension, independent of the systemic RAS.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:499991 CAPLUS
DOCUMENT NUMBER: 129:215100
TITLE: Alteration of intracellular Ca2+-handling and receptor regulation in hypertensive cardiac hypertrophy: insights from Ren2-transgenic rats
AUTHOR(S): Zolk, Oliver; Flesch, Markus; Nickenig, Georg; Schnabel, Petra; Bohm, Michael
CORPORATE SOURCE: Klinik III Innere Medizin, Univ. Koln, Cologne, 50924, Germany
SOURCE: Cardiovascular Research (1998), 39(1), 242-256
CODEN: CVREAU; ISSN: 0008-6363
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Abnormal intracellular Ca2+-handling appears to be a major cause of systolic and diastolic dysfunction in animals and humans with cardiac hypertrophy due to pressure overload and heart failure. However, the precise mechanisms which cause alteration of Ca2+-handling remain unclear. Several lines of evidence suggest that activation of neurohormonal systems may play a central role. In particular, widespread awareness of the importance of the renin-angiotensin system (RAS) has occurred since exptl. and clin. studies have detailed the efficacy of angiotensin-converting enzyme inhibitors in reducing morbidity and mortality in patients with left ventricular dysfunction. To evaluate in vivo the role of activated RAS in the regulation of (a) cardiac receptor expression and signal transduction mechanisms and (b) Ca2+ homeostasis, transgenic TG(mREN2)27 rats harboring the murine renin Ren2d gene were chosen. These animals develop fulminant hypertension and cardiac hypertrophy at an early age despite low levels of renin in the plasma. High expression of the transgene in the vasculature and the heart is associated with increased local formation of angiotensin II. In the Ren2-transgenic model alterations of β-adrenergic neuroeffector mechanisms, Ca2+-handling and α-adrenergic signal transduction are observed which are very similar to those observed in the myocardium of patients with end-stage heart failure. Moreover, treatment with specific inhibitors of the RAS, such as angiotensin-converting enzyme inhibitors or angiotensin II-receptor antagonists, largely reversed these defects. Studies on TG(mREN2)27 rats may provide new insights into the pathogenesis of hypertensive heart disease and mechanisms which promote disease progression to end-stage heart failure and also may have important implications with regard to therapeutics of heart failure in man.
REFERENCE COUNT: 144 THERE ARE 144 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:293011 CAPLUS
DOCUMENT NUMBER: 129:79800
TITLE: Renin-angiotensin system gene polymorphisms and left ventricular hypertrophy. The case against an association
AUTHOR(S): West, M. J.; Summers, K. M.; Wong, K. K.; Burstow, D. J.
CORPORATE SOURCE: Departments of Medicine and Cardiology, Prince Charles Hospital, University of Queensland, Chermside, QLD 4032, Australia
SOURCE: Advances in Experimental Medicine and Biology (1997), 432(Hypertension and the Heart), 117-122
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Plenum Publishing Corp.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 29 refs. There is accumulating evidence for assocn . between genetic polymorphisms of components of the renin angiotensin system (RAS), especially angiotensin-converting enzyme (ACE), and cardiovascular disease. However, there is lack of agreement that the ACE polymorphism is associated with left ventricular hypertrophy (LVH) in hypertension. A possible paradigm for the development of LVH involves the ACE gene polymorphism influencing cardiac mass by an action on plasma and/or tissue levels of angiotensin II. Such a model has exptl. support and provides the basis for examining the lack of agreement between studies. The finding of lack of association between RAS gene polymorphism and LVH may be due to methodol. problems, differences in genetic background between populations, interactions between genetic variants of RAS components or to the model being inappropriate. Low predictability of ACE genotype markers for LVH together with conflicting reports on the influence of RAS genetic variants on angiotensin II production suggests that the simple RAS paradigm may not apply for hypertension. Further information on the nature of the link between the ACE polymorphism and ACE regulation as well as the relation between the RAS and pathophysiol. of LVH is needed. At present there is insufficient evidence to accept ACE gene polymorphism as a susceptibility marker for LVH.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:805301 CAPLUS
DOCUMENT NUMBER: 128:97767
TITLE: Molecular mechanisms of angiotensin II in modulating cardiac function: intracardiac effects and signal transduction pathways
AUTHOR(S): Dostal, D. E.; Hunt, R. A.; Kule, C. E.; Bhat, G. J.; Karoor, V.; Mcwhinney, C. D.; Baker, K. M.
CORPORATE SOURCE: Geisinger Clinic, Weis Center for Research, Danville, PA, 17822, USA
SOURCE: Journal of Molecular and Cellular Cardiology (1997), 29(11), 2893-2902
CODEN: JMCDAY; ISSN: 0022-2828
PUBLISHER: Academic Press Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with .apprx.70 refs. Angiotensin II (Ang II), the effector peptide of the renin-angiotensin system (RAS), regulates volume and electrolyte homeostasis and is involved in cardiac and vascular cellular growth in humans and other species. This system, which has been conserved throughout evolution, plays an important role in cardiac and vascular pathol. associated with hypertension, coronary heart disease, myocarditis and congestive heart failure. The traditional RAS is viewed as a system in which circulating Ang II is delivered to target organs and cells. However, in the past decade, a local RAS has been described in cardiac cells, providing evidence for autocrine and paracrine pathways by which biol. actions of Ang II could be mediated. The critical actions of Ang II are mediated primarily through the AT1 G-protein (guanylyl nucleotide binding protein) coupled receptor. In addition to coupling to conventional G-protein signal transduction pathways, the AT1 receptor was recently shown to increase the tyrosine phosphorylation of several intracellular substrates, including the STAT (Signal Transducers and Activators of Transcription) family of novel transcription factors, in rat cardiac fibroblasts, myocytes and vascular smooth muscle cells, and AT1 receptor transfected CHO cells. It has been shown that Ang II stimulates the tyrosine phosphorylation and nuclear translocation of Stat1 (Stat 91) and Stat3 (Stat 92). Angiotensin II acting directly through the AT1 receptor, induces the formation of a complex of STAT proteins termed SIF (sis-inducing factor) which binds the DNA sequence, SIE (sis-inducing element) present in the promoter element of many genes. This provides evidence for a direct role of Ang II in mediating inflammatory and remodeling responses through the JAK-STAT pathway. Thus, it is likely that the JAK-STAT pathway has an important role in Ang II-mediated effects on gene transcription, cardiac and vascular cellular growth/development, and inflammatory responses.
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:744739 CAPLUS
DOCUMENT NUMBER: 128:33174
TITLE: Pivotal role of the renin-angiotensin system in Lyon hypertensive rats
AUTHOR(S): Lantelme, Pierre; Lo, Ming; Luttenauer, Laurent; Sassard, Jean
CORPORATE SOURCE: Dep. Physiol. Pharmacol. Clinique Unite Propre Recherche l'Enseignement Superieur Associee 5014 Centre National Recherche Scientifique Faculte Pharmacie, Lyon, 69008, Fr.
SOURCE: American Journal of Physiology (1997), 273(5, Pt. 2), R1793-R1799
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors assessed the role of the renin-angiotensin system (RAS) in Lyon genetically hypertensive (LH) and normotensive (LN) rats by measuring (1) kidney renin and prorenin contents; (2) effects of early, prolonged angiotensin-converting enzyme (ACE) inhibition on blood pressure (BP) and regional hemodynamics; and (3) acute and chronic responses to angiotensin II (ANG II) and norepinephrine (NE). At the adult age, LH rats differed from LN rats by elevated BP, left ventricle weight, and vascular resistances, especially in the kidneys, associated with lower kidney renin and prorenin contents. ACE inhibition (perindopril, 3 mg·Kg-1·24 h-1 orally from 3 to 15 wk of age) suppressed the development of hypertension, cardiac hypertrophy, and the increase in renal vascular resistances. No specific hypersensitivity to ANG II could be disclosed in acute conditions. In perindopril-treated LH rats, a 4-wk infusion of ANG II (200 ng·kg-1·min-1) but not of NE (1,000 ng·kg-1·min-1) restored hypertension, mimicked the hemodynamic alterations seen in untreated LH rats, and produced a brief sodium retention. It is concluded that in LH rats, despite a low basal renin secretion, hypertension and hemodynamic abnormalities (1) are fully dependent on an active renin-angiotensin system and (2) may involve an enhancer sensitivity to the chronic effects of ANG II.

L8 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:202347 CAPLUS
DOCUMENT NUMBER: 126:249677
TITLE: Role of the renin-angiotensin system in the development of hypertensive left ventricular hypertrophy
AUTHOR(S): Shiojima, Ichiro; Yamazaki, Tsutomu; Komuro, Issei; Nagai, Ryozo; Yazaki, Yoshio
CORPORATE SOURCE: Third Department of Medicine, University of Tokyo School of Medicine, Tokyo, 113, Japan
SOURCE: Molecular and Cellular Mechanisms of Cardiovascular Regulation, [Sendai International Symposium on Molecular and Cellular Mechanisms of Cardiovascular Regulation], Sendai, May 10-12, 1995 (1996), Meeting Date 1995, 409-415. Editor(s): Endoh, Masao. Springer: Tokyo, Japan.
CODEN: 64DGAZ
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Previous studies have demonstrated that angiotensin II (AII) acts as a growth-promoting factor on cardiac myocytes and that treatment with angiotensin-converting enzyme (ACE) inhibitors induces reduction of left ventricular mass and suppression of ventricular remodeling. These results suggest that the renin-angiotensin system (RAS) may play an important role in the development of hypertensive left ventricular hypertrophy (LVH). Moreover, it has recently been demonstrated that gene expression of angiotensinogen and ACE is augmented in pressure-overloaded left ventricles, suggesting that endogenous AII produced by the activated cardiac RAS may contribute to the formation of LVH. To elucidate the role of the RAS in the progression of cardiac hypertrophy, we evaluated the effect of the type 1 AII receptor (AT1 receptor) antagonist on LVH in spontaneously hypertensive rats (SHR) and investigated the mol. mechanisms by which antagonism of AII receptors reduces cell hypertrophy of myocytes using the in vitro model of mech. stretching. In the in vivo study, we treated SHR with a nonpeptide AT1 receptor antagonist, TCV-116. Treatment with TCV-116 reduced anatomical left ventricular (LV) weight, echocardiog. LV wall thickness, transverse diameter of myocytes, and the relative amount of V3 myosin heavy-chain and interstitial collagen volume fraction. In the in vitro study, neonatal rat cardiomyocytes were cultured on deformable silicone dishes and mech. stretched with or without pretreatment of CV-11974, an active metabolite of TCV-116. Pretreatment of cultured cardiomyocytes with CV-11974 partially inhibited an increase in MAP kinase activity, c-fos gene expression and [3H] phenylalanine incorporation induced by stretching of cardiomyocytes. These results indicate that (1) the RAS plays a critical role not only in the development of hypertensive LVH but also in the ventricular remodeling associated with LVH, which subsequently leads to the impairment of cardiac function and (2) endogenous AII produced by the cardiac RAS contributes to the pathogenesis of LVH.

L8 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:157459 CAPLUS
DOCUMENT NUMBER: 126:181125
TITLE: Enalapril and losartan reduced cardiac mass and improved coronary hemodynamics in SHR
AUTHOR(S): Nunez, Eduardo; Hosoya, Kazuyoshi; Susic, Dinko; Frohlich, Edward D.
CORPORATE SOURCE: Hypertension Research Laboratories, Alton Ochsner Medical Foundation, New Orleans, LA, 70121, USA
SOURCE: Hypertension (Dallas) (1997), 29(1, Pt. 2), 519-524
CODEN: HPRTDN; ISSN: 0194-911X
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Among the multiple mechanisms postulated for the increased risk of hypertensive left ventricular hypertrophy (LVH), coronary hemodynamic alterations remain a strong possibility. This study was designed to compare the effects of treatment with an ACE inhibitor (enalapril) and an angiotensin AT1 receptor antagonist (losartan) on systemic and coronary hemodynamics and to determine whether the combination of these two renin-angiotensin system (RAS) inhibitors would be as or more effective in reducing mean arterial pressure (MAP), left ventricular (LV) mass, and improving coronary hemodynamics than either regimen alone. Thus, 23 wk old spontaneously hypertensive rats (SHR) were treated (12 wk) with tap water (C), enalapril (30 mg·kg-1·d-1), losartan (30 mg·kg-1·d-1), or their combination (15 mg·kg-1·d-1). Age-matched Wistar-Kyoto (WKY) rats served as normotensive controls. After 12 wk, systemic and coronary hemodynamics were determined (15 μm radiolabeled microspheres) at baseline, during maximal treadmill exercise, and during maximal dilation (dipyridamole). Enalapril and losartan equally reduced MAP and LV mass in association with a decreased total peripheral resistance. The RAS combination reduced MAP and LV mass more than either drug alone. Resting cardiac index and coronary blood flow (CBF) per unit of LV mass did not differ among the groups. Although enalapril did not improve coronary flow reserve (CFR), it diminished minimal coronary vascular resistance (MCVR); losartan improved both. However, the combination was more effective than either agent alone, reaching values close to normotensive WKY controls. In conclusion, these data demonstrated significantly impaired maximal CBF, CFR, and MCVR in untreated SHR, but losartan alone and in combination with enalapril improved systemic and coronary hemodynamics more than enalapril alone.

L8 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:216003 CAPLUS
DOCUMENT NUMBER: 102:216003
TITLE: Can inhibition of the renin-angiotensin system have a cardioprotective effect?
AUTHOR(S): Michel, Jean Baptiste; Dussaule, Jean Claude; Alhenc-Gelas, Francois; Corvol, Pierre; Menard, Joel
CORPORATE SOURCE: INSERM, Paris, Fr.
SOURCE: Journal of Cardiovascular Pharmacology (1985), 7(Suppl. 2), S75-S79
CODEN: JCPCDT: ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The inhibition of the renin [9015-94-5]-angiotensin [1407-47-2] system (RAS) has important effects on different parameters of left ventricular function. Chronic inhibition of the RAS avoids hypokalemia and K losses by increasing aldosterone release. This K-sparing effect is likely to prevent cardiac arrhythmia. Inhibition of the RAS reverses cardiac hypertrophy in renovascular and in spontaneously hypertensive rats (SHR), but not in DOCA-salt hypertensive rats. Inhibition of the RAS also reverses the decrease in myocardial contractility, as demonstrated by the reversion of isoenzyme profile of cardiac myosin in renovascular hypertensive rats. In DOCA-salt hypertensive rats, RAS inhibition has no effect on blood pressure or on cardiac contractility. Despite its peripheral vasodilatory property, inhibition of the RAS does not increase heart rate in relation to a direct neg. chronotropic effect of angiotensin II inhibition and to the absence of activation of the baroreflex system. When RAS is activated, its inhibition has a coronary vasodilatory effect, but this coronary vasodilation is associated with a decrease in perfusion pressure and with an increase in intrinsic cardiac contractility. Evidently, inhibition of RAS has no important beneficial effect on the O demand/O supply ratio in the myocardium distal to the coronary artery stenosis.

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L2          4306 S L1 AND DISEASE
L3          1048 S L2 AND (RAS)
L4             0 S L3 AND ASSPCIAT?
L5           323 S L3 AND ASSOCIAT?
L6           126 S L5 AND PY<2003
L7            56 S L6 AND HYPERTENSION?
L8            17 S L7 AND CARDIAC?

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